State of California

Board of Equalization
Office of the Chief Counsel – MIC:83

Memorandum

To: Honorable John Chiang, Chair
Honorable Claude Parrish, Vice Chairman
Ms. Betty T. Yee, Acting Board Member
Honorable Bill Leonard
Honorable Steve Westly

Date: October 6, 2005

From: Kristine Cazadd
Chief Counsel

Subject: Petition for Amendment of Sales and Use Tax Regulation 1591
Medicines and Medical Devices
Subdivisions (a)(9) and (b)
Cosmetic Procedures

Chief Counsel Matters – Tuesday, October 25, 2005

Background

On September 21, 2005, the law firm of Wilke, Fleury, Hoffelt, Gould & Birney LLP filed a petition pursuant to Government Code section 11340.6, requesting the Board to amend subdivisions (a)(9) and (b), both entitled "Medicines," of Regulation 1591, "*Medicines and Medical Devices*."[1] Exhibit A to the petition proposed language by which the section could be amended. The law firm filed the petition on behalf of the California Society of Dermatology and Dermatologic Surgery, the California Society of Plastic Surgery, the California Academy of Ophthalmology, and the California Medical Association (hereafter, collectively, petitioner). Copies of the petition, Government Code section 11340.6 and Regulation 1591 are attached.

This matter is scheduled to be heard at the Chief Counsel Rulemaking Calendar on October 25, 2005.

According to the petition, numerous California physicians are being audited by the Board and assessed deficiencies. The deficiencies are assessed on the ground that sales of Botox® and Botox® Cosmetic are subject to tax when the eventual application of the product is for cosmetic purposes, mainly for treatment of skin wrinkles.

Under Revenue and Taxation Code section (Section) 6369, interpreted and implemented by Regulation 1591, sales or other transfers of medicines as defined in the statute are not subject to tax if they are sold or otherwise transferred pursuant to transactions specified in the statute. Section

[1] The petition mainly concerns subdivision (a)(9) of Regulation 1591. The petition only asks the Board to add to subdivision (b) a cross-reference to an amended subdivision (a)(9).

6369, subdivision (b), provides that the term "medicine" means "any substance or preparation intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment, or prevention of disease and commonly recognized as a substance or preparation intended for that use."

Grounds for the Petition

The grounds advanced in the petition are as follows:

1. **The methods of transfer of Botox® and Botox® Cosmetic come within the provisions of Section 6369, subdivision (a).**

Petitioner asserts that Botox® and Botox® Cosmetic are prescribed for the treatment of a human being by a person authorized to prescribe the medicines and are dispensed on a prescription filled by a registered pharmacist in accordance with the law or are furnished by a licensed physician and surgeon, dentist, or podiatrist to his or her own patient for treatment of the patient as required by Section 6369, subdivision (a)(1) and (2), and Regulation 1591, subdivision (d)(1) and (2).

2. **Botox® and Botox® Cosmetic Qualify as Medicines under Regulation 1591, subdivision (a)(9).**

Petitioner asserts that Botox® and Botox® Cosmetic are "substance[s] or preparation[s] intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment, or prevention of disease and commonly recognized as [substances] or preparation[s] intended for that use" within the meaning of Regulation 1591, subdivision (a)(9).

3. **The Federal Food and Drug Administration (FDA) Recognizes Glabellar (Frown) Lines as a Medical Condition.**

Petitioner alleges that the FDA has ruled that the FDA has termed frown lines as a "medical condition that is not serious" for the purposes of the Federal Food and Drug Act. Petitioner asserts that the Board's position regarding the use of Botox® and Botox® Cosmetic for "cosmetic purposes" is at odds with the federal regulatory approval of their use.

4. **The Board is Required to Broadly Construe Products Not Subject to Taxation.**

Citing the case of *Purdue Frederick Co. v. State Bd. of Equalization* (1990) 218 Cal.App.3d 1021, petitioner argues that the Board is required to construe the definition of medicines broadly to include Botox® and Botox® Cosmetic.

5. **Board Publications Advise Taxpayers that Sales of Substances "Commonly Recognized" as Medicines Are Tax Exempt.**

Board publications state that sales of prescription medicines are exempt from tax under specified conditions common in the health arenas. They also state that sales of "substances commonly recognized as medicines" are exempt from tax.

Options for Board Action

Pursuant to Government section Code 11340.7 (copy attached), upon receipt of a petition requesting the amendment or repeal of a regulation, the Board shall:

1. Deny each petition, in whole or in part, indicating in writing why the Board has reached its decision on the merits of the petition; or
2. Initiate the rulemaking process and schedule the matter for a public hearing in accordance with the rulemaking provisions of the Administrative Procedures Act (Gov. Code, § 11346 et seq.).

If the Board schedules the matter for public hearing it may, prior to setting the public hearing date and authorizing publication of the notice of hearing, hold public discussions of the proposal. (Gov. Code, § 11346.45.) For example, the Board may refer the matter to the Business Taxes Committee for the full or an abbreviated version of that process.

Furthermore, the Board may grant any other relief or take other such action it may determine to be warranted by the petition. (Gov. Code, § 11340.7, subd. (b).)

The decision of the Board regarding the petition is required to be in writing and to include the reasons therefor. The decision must be transmitted to the Office of Administrative Law for publication in the California Regulatory Notice Register. (Gov. Code, § 11340.7, subd. (d).)

Staff Recommendation

It is Staff's position that the proposed language provides a reasonable basis on which to resolve this issue. Defining "medicines" to include any product approved by the FDA "to diagnose, cure, mitigate, treat or prevent any disease, illness or medical condition" would provide a bright-line test for audit purposes, which will promote audit efficiency. Moreover, such an approach will avoid involving our audit staff in activities related to confidential patient records. Additionally, since Botox® and Botox® Cosmetic have only been approved for use on frown lines since 2002, little, if any, tax has been collected with respect to Botox® transactions. Accordingly, staff believes the revenue impact of this proposal would be minimal. Staff does not believe that the proposed language would impact any other transactions for which the Sales and Use Tax Department currently assesses tax.

Additional Information

Staff is available to provide additional information and to render whatever assistance the Board may require in making its decision. If you have any questions on these matters, please contact Acting Assistant Chief Counsel, Selvi Stanislaus at (916) 324-2579.

KC:ef

Attachments: Petition
Government Code Section 11340.6
Government Code Section 11340.7
Regulation 1591, "Medicines and Medical Devices"

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BY HAND DELIVERY

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RE: Petition for Amendment of Title 18, California Code of Regulations, Section 1591(a)(9) and (b) – Medicines and Medical Devices

Dear Ms. Olson:

The purpose of this letter is to petition the California State Board of Equalization (the "Board" or "BOE"), pursuant to Government Code section 11340.6, to amend Title 18, California Code of Regulations, Section 1591(a)(9) and (b) relating to the inapplicability of state sales and use tax to medicines. A "redlined" version of the pertinent portion of the regulation, with the proposed text of the amendment noted by underscore, is attached hereto as Exhibit "A." The basis for this petition is outlined below.

This petition is submitted, jointly and collectively, on behalf of the parties affirming below, including the California Society of Dermatology and Dermatologic Surgery, the California Society of Plastic Surgery, the California Academy of Ophthalmology and the California Medical Association (hereafter referred to, collectively as "California Medicine").

BOE ACTIONS NECESSITATE REGULATORY CLARIFICATION

It has come to the attention of California Medicine, that numerous California physicians are being subjected to audits by the BOE. The audits are not representative of uniform policy within the BOE audit staff, as we understand it. Additionally, the audits do not implement any new policy setting action by the Board, nor even a recent restatement of existing policy, regarding sales and use tax applicability to medicines administered in California. Rather, this tax policy arises exclusively through a determination of tax applicability on the part of BOE staff.

In the course of these audits, BOE field auditors are asserting – erroneously - that these physicians should have been collecting and remitting state sales and use tax on all administrations (i.e., "sales") of the prescription medicine, Botox® and/or Botox® Cosmetic, when the eventual application of the medicine is for a so-called "cosmetic purpose." BOE audit staff contend that "cosmetic" uses do not rise to the level of treatment of a medical condition under current BOE regulations (18 CCR 1591(a)(9)). Use of a medicine for the treatment of a condition that audit staff agree is a "medical condition," apparently is, *per se*, exempt from application of the state sales and use tax under both state sales and use tax law, and the BOE's own implementing regulation. Not so, however, is physician treatment of a condition that audit staff do not agree is a "medical condition," or a condition of sufficient severity to warrant consideration as a "medical condition." California Medicine is apprised that physician administration of Botox® and Botox® Cosmetic for treatment of skin wrinkles has been singled out.

The BOE position in these audits, according to audit staff, is that such treatments constitute a nonmedical use of a prescription medicine under both California Revenue and Taxation Code Section 6369 (b) and BOE Regulation 1591(a)(9). California Medicine has learned that the same position has been expressed to those physicians who contacted BOE regarding the recent, and continuing, "tax amnesty" program, in an effort to ascertain whether those physicians should elect to participate in the amnesty program.

BOE ACTIONS DEFY THE PLAIN READING OF EXISTING LAW

Revenue and Taxation Code Section 6369:

Revenue and Taxation Code Section 6369 plainly states:

"(a) There are exempted from the taxes imposed by this part the gross receipts from the sale in this state of, and the storage, use, or other consumption in this state of, medicines:

(1) **Prescribed for the treatment of a human being by a person authorized to prescribe the medicines**, and dispensed on prescription filled by a registered pharmacist in accordance with law.

(2) **Furnished by a licensed physician and surgeon, dentist, or podiatrist to his or her own patient for treatment of the patient**." (Emphases added)

Botox® and Botox® Cosmetic, as the enclosed exhibits clearly establish, precisely fit the four corners of the statute, as do the audited physician applications of the product.

Stretching credulity, the BOE audit positions can only proceed from an assertion that under subdivision (b) of this section, Botox® is not being used in a manner that qualifies the use for exemption from the tax:

"(b) 'Medicines' as used in this section, means any substance or preparation intended for use by external or internal application to the human **body in the diagnosis, cure, mitigation, treatment, or prevention of disease** and commonly recognized as a substance or preparation intended for that use." (Emphasis added.)

BOE Regulation 1591 (18 CCR §1591):

BOE regulation 1591 tracks the enabling statute almost *verbatim*:

"(d) APPLICATION OF TAX—IN GENERAL. Tax applies to retail sales, including over-the-counter sales of drugs and medicines, and other tangible personal property by pharmacists and others. However, **tax does not apply to the sale or use of medicines when sold or furnished under one of the following conditions**:

(1) **prescribed for the treatment of a human being by a person authorized to prescribe the medicines**, and dispensed on prescription filled by a pharmacist in accordance with law, or

(2) **furnished by a licensed physician, dentist or podiatrist to his or her own patient for treatment of the patient**...." (Emphases added)

The regulation's definition of medicines, on which BOE rests its incorrect interpretation, closely tracks the enabling statute, as well:

"(9) MEDICINES. "Medicines" means **any substance or preparation intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease** and which is commonly recognized as a substance or preparation intended for that use. The term medicines also includes certain articles, devices, and appliances as described in subdivision (b) of this regulation." (Emphasis added.)

In short, ignoring a plain reading of the applicable exemption, the BOE contends that the treatment of wrinkles does not qualify for the exemption. However, BOE appears to be applying an unstudied, layperson's view of the treatments for which Botox® and Botox® Cosmetic are used, rather than engaging in simple research that would have enabled the BOE to avoid imposing this circumstance on California physicians altogether. Unfortunately, this patently incorrect position has led to considerable alarm and expense among physicians in California, necessitating this petition by California Medicine.

Ironically, neither BOE's regulation, nor authorizing statute in this matter, provide a definition of "disease" or "medical condition," leaving BOE audit staff "free rein" to apply completely subjective and unscientific views regarding disease or medical conditions to support *ad hoc* tax policy, even in the face of such authority as described hereafter.

FDA Treatment Approvals of Botox® and Botox® Cosmetic in the United States

Readily available on the U.S. Food and Drug Administration's (FDA) website is the approval history for Botox® and Botox® Cosmetic in the United States. In April 2002, the FDA expanded the use of Botox® and stated,

> "Botulinum Toxin Type A (BOTOX) is currently licensed for the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia and the treatment of strabismus and blepharospasm associated with dystonia. Under this approval, Botulinum Toxin Type A (BOTOX COSMETIC) may be used for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients < 65 years of age." (Exhibit "1;" Emphasis added.)

In its associated *Talk Paper* issued at the same time, the FDA described its approval as follows:

> "FDA today announced the approval of Botulinum Toxin Type A (Botox Cosmetic) to temporarily improve the appearance of moderate to severe frown lines between the eyebrows (glabellar lines), a medical condition that is not serious. The product's manufacturer, Allergan, Inc., Irvine, California, is now allowed to market Botulinum Toxin Type A for this new indication." (Exhibit "2;" Emphasis added.)

Also included as exhibits are the FDA-issued documents authorizing specific medical uses of Botox® and Botox® Cosmetic. (Exhibits "3" through "5")

The BOE's claim that because Botox® Cosmetic is being used for "cosmetic purposes," it does not qualify for sales tax exemption typical of prescription drugs, is completely at odds with the federal regulatory approval for its use in the United States.

BOE HAS RECEIVED JUDICIAL DIRECTION TO BROADLY CONSTRUE THOSE PRODUCTS NOT SUBJECT TO TAXATION

In 1990, the California Court of Appeal rendered an opinion whereby the Court provided guidance relative to its interpretation of California Revenue and Taxation Code Section 6369 and BOE regulation 1591. In Purdue Frederick Company v. State Board of Equalization, 218 Cal. App. 3d 1021 (March 14, 1990), the Court was asked to determine on appeal whether Betadine® Surgical Scrub (Betadine®), an antiseptic, microbicidal, sudsing skin cleanser, manufactured by Purdue was tax exempt as a "medicine."

In the Purdue case, the BOE took the position that Betadine® was not a "medicine" for purposes of exemption from sales tax in accordance with Section 6369 because it was not used to treat a "human being." Purdue paid the tax and filed an action for refund. The BOE determined that 20% of the time Betadine® was used by those involved in the treatment of patients as a cleansing agent and not directly on patients. In that regard, the BOE took the position that 20% of the sales of Betadine® was not a "medicine" and, therefore, subject to sales tax.

The Court held that the BOE's analysis of Section 6369 as applied to Betadine®'s uses were too narrow and internally inconsistent. The Court held that Sections (a)(2) through (a)(6) were added to expand the exemption to a larger group of "medicines" rather than limit the definition of "medicine" as suggested by the BOE. The Court noted that the BOE's interpretation of "treatment" as applied to Betadine® and noted at Section 6369(a)(4) caused a conflict with Section 6369(b) which refers to the "application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease." The Court further stated that treatment means "the application or an instance of treating someone or something." The Court continued and noted that to "treat is to care for or deal with medically or surgically and to act upon with some agent especially to improve or alter" a patient's appearance or condition.

Clearly, the Court's definition of the word "treatment" as used in Section 6369(b) includes as "medicines" Botox® and/or Botox Cosmetic. Botox® and/or Botox Cosmetic® is an internal agent used by a physician to "treat" a patient's glabellar lines and cervical dystonia conditions. Upon application, Botox® and/or Botox Cosmetic unquestionably alters a patient's appearance by reducing the number and extent of glabellar lines.

Furthermore, in making its decision, the Court reviewed the legislative history of Section 6369. The Court noted that originally Section 6369 was limited to an exemption for medicines now contained in subdivision (a)(1), those prescribed by an authorized person and dispensed on

prescription. (Stats 1961, ch 866 Section 1, p. 2273.) In 1962, the Legislature added those exemptions now contained in subdivision (a)(2) and (a)(3). In 1963, the Legislature restructured section 6369 by numbering the different types of exempt medicines, adding the exemptions contained in subdivisions (a)(4) and (a)(5) and changing the definition of medicine. The Court reasoned that the changes to Section 6369 evidence a clear legislative intent to expand the scope of exempt "medicine." The Court held that the BOE's interpretation of Section 6369 in terms of the definition of "treatment" was too narrow and restrictive. In this matter, the BOE again is narrowly construing Section 6369 to exclude a "medicine (e.g. Botox® and/or Botox Cosmetic®) without any legislative support for such an interpretation.

Given the Court's holding in Purdue and the uses of Botox® and/or Botox Cosmetic® to treat glabellar lines and cervical dystonia, the BOE's apparent position is clearly inconsistent with California's common law and Section 6369. While Botox® and/or Botox Cosmetic® are typically not used to treat a life threatening or serious medical conditions, they are, nonetheless, clearly "medicine" as it is defined under California law.

BOE PUBLICATIONS ADVISE CALIFORNIA TAXPAYERS THAT SUBSTANCES "COMMONLY RECOGNIZED" AS MEDICINES ARE TAX EXEMPT

In addition to its governing statute on the matter, and its implementing regulation, the BOE's published guidance to taxpayers in California regarding exemptions and exclusions from state sales and use tax broadly and plainly describes those exemptions and exclusions, by category, when specifically addressing prescription medicines:

> "PRESCRIPTION MEDICINES — Sales of medicines are exempt from sales and use taxes if 1) prescribed for treatment of human beings and dispensed by a registered pharmacist; 2) furnished by or sold to a licensed physician and surgeon, podiatrist, or dentist for patient treatment; 3) furnished by a health facility for patient treatment pursuant to the order of a licensed physician; 4) sold to this state or any political subdivision or municipal corporation for use in treating human beings; 5) dispensed by prescription for the treatment of human beings and furnished without charge by a pharmaceutical manufacturer or distributor to a doctor, a health facility for the treatment of human beings, or to an institution of higher education for instruction or research; 6) furnished by a medical facility or clinic operated by this state or any political subdivision or municipal corporation; or 7) sold to outpatient clinics, as defined under Health and Safety Code 1200, for the treatment of any person pursuant to the order of a licensed physician and surgeon, dentist, and podiatrist. In addition to substances commonly recognized as medicines, the following items are specifically included in the definition of "medicine" for sales and use tax purposes:...." *(Sales and Use Taxes: Exemptions and Exclusions California Revenue and Taxation Code Part 1, Division 2" May 2003 Publication No. 61 • LDA; Section A, Page 2; Emphases added.)*

The guidance expressly provides that sales of medicines are exempt from sales and use taxes, under specified conditions common in the health care arena – prescription for human treatment and dispensing through pharmacies, and direct sale to physicians "for patient treatment...." No further parsing of the explanation and guidance to taxpayers is provided. Clearly, none is needed.

Augmenting this basic guidance, the expansive introduction to devices and products that are also clearly exempt from the state sales and use tax, the BOE guidance to taxpayers states, plainly, "In addition to substances commonly recognized as medicines, the following items [are also exempt]...."

REGULATORY CLARIFICATION IS NEEDED TO AVOID REPEATED MISAPPLICATIONS OF SALES AND USE TAX TO BOTOX®/BOTOX® COSMETIC

The leadership of California Medicine respectfully submits its petition for regulatory clarification addressing a clear need to avoid repeated misapplications of state sales and use tax on the instant product(s) and those which may also have secured federal FDA recognition as "medicine(s)" approved for sales and use in the United States. The regulatory clarification is needed to promptly reverse the current *ad hoc* BOE policy in this respect and address the subjective application of tax to medicines specifically approved as such in the United States by the FDA, as well as being "commonly recognized" as such.

The Board, in accepting this regulatory petition for public review and, ultimately adoption, may move promptly to correct the erroneously held position developed by BOE staff, may publicize it through its public relations and taxpayer education channels, and may educate its personnel who may have offered, or may be currently offering, incorrect advice to inquiring taxpayers.

California Medicine respectfully requests acceptance of this petition by the Board of the California State Board of Equalization to reverse and modify the current and ongoing impact being visited by the BOE upon California physicians.

Respectfully Submitted,

John R. Valencia

On Behalf Of

Jack Resneck, Jr., M.D., President-elect
California Society of Dermatology
And Dermatologic Surgery

Malcolm Paul, M.D., President
California Society of Plastic Surgery

Ron Morton, M.D., FACS, President
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Dustin Corcoran, Vice President
Government Relations
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JRV: df
Enclosures (6)
162425.2

Exhibit A

State of California

BOARD OF EQUALIZATION

SALES AND USE TAX REGULATIONS

REGULATION 1591. MEDICINES AND MEDICAL DEVICES (*Relevant Excerpts).

Reference: Sections 6006 and 6369 Revenue and Taxation Code.

(a) DEFINITIONS.

(1) ADMINISTER. "Administer" means the direct application of a drug or device to the body of a patient or research subject by injection, inhalation, ingestion, or other means.

(2) DISPENSE. "Dispense" means the furnishing of drugs or devices upon a prescription from a physician, dentist, optometrist, or podiatrist. Dispense also means and refers to the furnishing of drugs or devices directly to a patient by a physician, dentist, optometrist, or podiatrist acting within the scope of his or her practice.

(3) FURNISH. "Furnish" means to supply by any means, by sale or otherwise.

(4) HEALTH FACILITY. "Health Facility" as used herein has the meaning ascribed to the term in section 1250 of the Health and Safety Code, which provides that:

"As used in this chapter 'health facility' means any facility, place or building that is organized, maintained, and operated for the diagnosis, care, prevention, and treatment of human illness, physical or mental, including convalescence and rehabilitation and including care during and after pregnancy, or for any one or more of these purposes, for one or more persons, to which the persons are admitted for a 24-hour stay or longer...."

(5) PHARMACIST. "Pharmacist" means a person to whom a license has been issued by the California State Board of Pharmacy, under the provisions of section 4200 of the Business and Professions Code, except as specifically provided otherwise in Chapter 9 of the Pharmacy Law."

(6) PHARMACY. "Pharmacy" means an area, place, or premises licensed by the California State Board of Pharmacy in which the profession of pharmacy is practiced and where prescriptions are compounded. Pharmacy includes, but is not limited to, any area, place, or premises described in a license issued by the California State Board of Pharmacy wherein controlled substances, dangerous drugs, or dangerous devices are stored, possessed, prepared, manufactured, derived, compounded, or repackaged, and from which the controlled substances, dangerous drugs, or dangerous devices are furnished, sold, or dispensed at retail. Pharmacy shall not include any area specifically excluded by paragraph (b) of section 4037 of the Business and Professions Code.

(7) PRESCRIPTION. "Prescription" means an oral, written, or electronic transmission order that is issued by a physician, dentist, optometrist, or podiatrist licensed in this state and given individually for the person or persons for whom ordered. The order must include all of the following:

(A) The name or names and address of the patient or patients.

(B) The name and quantity of the drug or device prescribed and the directions for use.

(C) The date of issue.

(D) Either rubber stamped, typed, or printed by hand or typeset, the name, address, and telephone number of the prescriber, his or her license classification, and his or her federal registry number, if a controlled substance is prescribed.

(E) A legible, clear notice of the conditions for which the drug is being prescribed, if requested by the patient or patients.

(F) If in writing, signed by the prescriber issuing the order.

(8) PHYSICIANS, DENTISTS, OPTOMETRISTS, AND PODIATRISTS. "Physicians," "dentists," "optometrists," and "podiatrists" are persons authorized by a currently valid and unrevoked license to practice their respective professions in this state. "Physician" means and includes any person holding a valid and unrevoked physician's and surgeon's certificate or certificate to practice medicine and surgery, issued by the Medical Board of California or the Osteopathic Medical Board of California and includes an unlicensed person lawfully practicing medicine pursuant to section 2065 of the Business and Professions Code, when acting within the scope of that section.

(9) MEDICINES. "Medicines" means ***(a) any product approved to diagnose, cure, mitigate, treat or prevent any disease, illness or medical condition by the U.S. Food and Drug Administration, or (b)*** any substance or preparation intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease and which is commonly recognized as a substance or preparation intended for that use. The term medicines also includes certain articles, devices, and appliances as described in subdivision (b) of this regulation.

(b) "MEDICINES." ~~:~~ ***In addition to the definition set forth in subdivision (a)(9) of this section, t***he term "medicines" means and includes the following items:

(1) PREPARATIONS AND SIMILAR SUBSTANCES. Preparations and similar substances intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease and which are commonly recognized as a substance or preparation intended for such use qualify as medicines. Tax does not apply to the sale or use of such medicines sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

"Preparations and similar substances" include, but are not limited to, drugs such as penicillin, and other antibiotics, "dangerous drugs" (drugs that require dispensing only on prescription); alcohol (70% solution) and isopropyl; aspirin; baby lotion, oil, and powder; enema preparations; hydrogen peroxide; lubricating jelly; medicated skin creams; oral contraceptives; measles and other types of vaccines; topical creams and ointments; and sterile nonpyrogenic distilled water. Preparations and similar substances applied to the human body in the diagnosis, cure, mitigation, treatment, or prevention of disease qualify as medicines. "Preparations and similar substances" also include Total Parenteral Nutrition (also called TPN), Intradialytic Parenteral Nutrition (also called IDPN), and food provided by way of enteral feeding, except when the TPN, IDPN, or food provided by enteral feeding qualifies as a meal under Regulation 1503. For purposes of this regulation, TPN, IDPN, and enteral feeding are means of providing complete nutrition to the patient; TPN and IDPN are provided in the form of a collection of glucose, amino acids, vitamins, minerals, and lipids, TPN being administered intravenously to a patient who is unable to digest food through the gastrointestinal tract and IDPN being administered to hemodialysis patients as an integral part of the hemodialysis treatment; enteral feeding is the feeding of the patient directly into the gastrointestinal tract.

2) PERMANENTLY IMPLANTED ARTICLES. Articles permanently implanted in the human body to assist the functioning of, as distinguished from replacing all or any part of, any natural organ, artery, vein or limb and which remain or dissolve in the body qualify as medicines. An article is considered to be permanently implanted if its removal is not otherwise anticipated. Tax does not apply to the sale or use of articles permanently implanted in the human body to assist the functioning of any natural organ, artery, vein or limb and which remain or dissolve in the body when such articles are sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

Permanently implanted articles include, but are not limited to, permanently implanted artificial sphincters; bone screws and bone pins, dental implant systems including dental bone screws and abutments; permanently implanted catheters; permanently implanted hydrocephalus devices and their implanted pressure regulating components; implanted defibrillators and implanted leads; pacemakers; tendon implants; testicular gel implants; and ear implants. Sutures are also included whether or not they are permanently implanted. A non-returnable, nonreusable needle fused or prethreaded to a suture is regarded as part of the suture.

Implantable articles that do not qualify as "permanently" implanted medicines include, but are not limited to, Chemoport implantable fluid systems; Port-a-Cath systems used for drug infusion purposes; disposable urethral catheters; temporary myocardial pacing leads used during surgery and recovery; and defibrillator programmer and high voltage stimulator used with an implanted defibrillator. The sale or use of these items is subject to tax.

(3) ARTIFICIAL LIMBS AND EYES. Artificial limbs and eyes, or their replacement parts, including stump socks and stockings worn with artificial legs and intraocular lenses for human beings, qualify as medicines as provided by Revenue and Taxation Code section 6369 (c)(5). Tax does not apply to the sale or use of these items when sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

(4) ORTHOTIC DEVICES. Orthotic devices and their replacement parts, other than orthodontic devices, designed to be worn on the person of the user as a brace, support or correction for the body structure are medicines

(c) EXCLUSIONS FROM THE DEFINITION OF "MEDICINES."

Except as otherwise provided in subdivision (b), the following items are specifically excluded from the definition of medicines:. Sales of these items are subject to tax in the same manner as any other sale of tangible personal property.

(1) Orthodontic, prosthetic (except as described in subdivision (b)(6)), auditory, ophthalmic or ocular devices or appliances.

(2) Articles which are in the nature of splints, bandages, pads, compresses, supports, dressings, instruments, apparatus, contrivances, appliances, devices or other mechanical, electronic, optical or physical equipment or article or the component parts and accessories thereof. "Medicines" does not include arch supports, cervical pillows, exercise weights (boots or belts), hospital beds, orthopedic shoes and supportive devices (unless an integral part of a leg brace or artificial leg), plastazote inserts, plastazote shoes, plastic shoes (custom or ready-made), sacro-ease seats, shoe modifications, spenco inserts, traction units (other than those fully worn on the patient), thermophore pads, or foot orthoses.

(3) Any alcoholic beverage the manufacture, sale, purchase, possession or transportation of which is licensed and regulated by the Alcoholic Beverage Control Act (Division 9, commencing with section 23000, of the Business and Professions Code).

(d) APPLICATION OF TAX—IN GENERAL.

Tax applies to retail sales, including over-the-counter sales of drugs and medicines, and other tangible personal property by pharmacists and others. However, tax does not apply to the sale or use of medicines when sold or furnished under one of the following conditions:

(1) prescribed for the treatment of a human being by a person authorized to prescribe the medicines, and dispensed on prescription filled by a pharmacist in accordance with law, or

(2) furnished by a licensed physician, dentist or podiatrist to his or her own patient for treatment of the patient, or

(3) furnished by a health facility for treatment of any person pursuant to the order of a licensed physician, dentist or podiatrist, or

(4) sold to a licensed physician, dentist, podiatrist or health facility for the treatment of a human being, or

(5) sold to this state or any political subdivision or municipal corporation thereof, for use in the treatment of a human being; or furnished for the treatment of a human being by a medical facility or clinic maintained by this state or any political subdivision or municipal corporation thereof, or

(6) effective January 1, 1995, furnished by a pharmaceutical manufacturer or distributor without charge to a licensed physician, surgeon, dentist, podiatrist, or health facility for the treatment of a human being, or to an institution of higher education for instruction or research. Such medicine must be of a type that can be dispensed only: (a) for the treatment of a human being, and (b) pursuant to prescriptions issued by persons authorized to prescribe medicines. The exemption provided by this subdivision applies to the constituent elements and ingredients used to produce the medicines and to the tangible personal property used to package such medicines.

(2) LICENSED PHYSICIAN, DENTIST OR PODIATRIST. Tax does not apply to a specific charge made by a licensed physician, dentist or podiatrist to his or her own patient for medicines furnished for the treatment of the patient. Tax also does not apply to sales of medicines to licensed physicians, dentists or podiatrists for the treatment of a human being regardless of whether the licensed physician, dentist or podiatrist makes a specific charge to his or her patient for the medicines furnished.

(3) HEALTH FACILITY Tax does not apply to sales of medicines by a health facility (as defined in suddivision (a)(4)) for the treatment of any person pursuant to the order of a licensed physician, dentist or podiatrist. Tax does not apply to sales of medicines to a health facility for the treatment of a human being regardless of whether or not a specific charge is made for the medicines.

(4) PHARMACEUTICAL MANUFACTURER OR DISTRIBUTOR. Tax does not apply to the storage, use or consumption of medicines furnished by a pharmaceutical manufacturer or distributor without charge to a licensed physician, surgeon, dentist, podiatrist, or health facility for the treatment of a human being or furnished without charge to an institution of higher education for instruction or research provided the medicines furnished are of a type that can be dispensed only (1) on prescription by persons authorized to prescribe and (2) for the treatment of a human being. The exemption from tax includes the costs of the materials used to package the "sample" medicines, such as bottles, boxes, blister packs, patches impregnated with medicines, or pre-filled syringes, and the elements and ingredients used to produce the "samples" whether or not such items are purchased under a resale certificate in this state or outside this state. When a pre-filled syringe or other such delivery device is used to package and contain a sample medicine (i.e., pre-filled with the medicine) as well as to inject or otherwise administer the medicine to the patient, the exemption from tax will not be lost due to the fact that the device is used for a dual purpose. However, the use of empty syringes or other such delivery devices, furnished to the licensed physician separately or included in the packages with the medicines, is subject to tax.

This exemption applies in the same manner to the use of clinical trial medicines during the United States Food and Drug Administration's drug development and approval process. "Clinical trial medicines" are substances or preparations approved as "Investigational New Drugs" by the United States Food and Drug Administration intended for treatment of, and application to, the human body, which are furnished by a pharmaceutical developer, manufacturer, or distributor to a licensed physician and subsequently dispensed, furnished, or administered pursuant to the order of the licensed physician. "Clinical trial medicines" do not include placebos. Placebos are not used for the treatment of a human being and, as such, do not qualify for the exemption provided under this subdivision. Thus, the use of placebos is subject to tax.

Proposed Changes

"(9) MEDICINES. "Medicines" means ***(a) any product approved to diagnose, cure, mitigate, treat or prevent any disease, illness or medical condition by the U.S. Food and Drug Administration, or (b)*** any substance or preparation intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease and which is commonly recognized as a substance or preparation intended for that use. The term medicines also includes certain articles, devices, and appliances as described in subdivision (b) of this regulation.

(b) "MEDICINES." ~~T~~ ***In addition to the definition set forth in subdivision (a)(9) of this section, t*** he term "medicines" means and includes the following items:...."

160900.3

Exhibit 1

Product Approval Information - Licensing Action

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

April 12, 2002

Submission Tracking No. (STN): BL 103000/5000

Mr. Peter A. Kresel
Allergan, Inc.
2525 Dupont Drive
P.O. Box 195
Irvine, CA 92713-9534

Dear Mr. Kresel:

The Supplement to your License Application, for Botulinum Toxin Type A to include the indication of treatment of glabellar lines, has been approved.

Under this approval, Botulinum Toxin Type A will be marketed and labeled for this indication as BOTOX COSMETIC.

Botulinum Toxin Type A (BOTOX) is currently licensed for the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia and the treatment of strabismus and blepharospasm associated with dystonia. Under this approval, Botulinum Toxin Type A (BOTOX COSMETIC) may be used for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients $\leq$ 65 years of age.

Under this approval, BOTOX COSMETIC shall be supplied, in vials, as a lyophilized formulation at a dose of 100 U per vial and the expiration dating period shall be 24 months when stored at -5°C to -20°C.

We acknowledge your March 11, 2002, submission of the final report for reproductive toxicity testing studies to BB IND XXXX. This submission is currently under review and we reserve the right to comment further on the contents of that submission and request further revisions to the labeling for BOTOX COSMETIC as warranted.

We acknowledge your commitment of March 26, 2002, to review the post-marketing adverse event surveillance data after one year of commercial distribution and propose revised labeling as warranted.

We have reviewed your request for a waiver from the requirement to assess the safety and effectiveness of the product in pediatric populations. Please be advised that a waiver for this application is granted under 21 CFR 601.27.

This information will be placed in your License Application File for this product.

Changes in the manufacturing process, manufacturing facility, product testing, packaging or labeling for Botulinum Toxin Type A (BOTOX and BOTOX COSMETIC) may require the submission of a supplement to your biologics license application for review and approval prior to implementation.

It is required that adverse experience reports be submitted in accordance with the adverse events reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, MD 28052-1448.

It is required that reports of errors and accidents in manufacture be submitted in accordance with the error and accident reporting requirements for licensed biological products (21 CFR 600.14). All error and accident reports should be identified promptly according to 21 CFR 600.14 and submitted to the Director, Office of Compliance, Center for Biologics Evaluation and Research, HFM-600, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim or superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Sincerely yours,

--- signature ---

Karen L. Goldenthal, M.D.
Director
Division of Vaccines and Related Products Applications
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

Last Updated: 4/14/2002

Back to Top Back to Index

Date created: September 25, 2003

Exhibit 2

U.S. Food and Drug Administration

FDA Talk Paper

FDA Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available.

T02-20
April 15, 2002

Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

FDA APPROVES BOTOX TO TREAT FROWN LINES

FDA today announced the approval of Botulinum Toxin Type A (Botox Cosmetic) to temporarily improve the appearance of moderate to severe frown lines between the eyebrows (glabellar lines), a medical condition that is not serious. The product's manufacturer, Allergan, Inc., Irvine, California, is now allowed to market Botulinum Toxin Type A for this new indication.

Botulinum Toxin Type A is a protein produced by the bacterium *Clostridium botulinum*. When used in medical settings as an injectable form of sterile, purified botulinum toxin, small doses of the toxin are injected into the affected muscles and block the release of the chemical acetylcholine that would otherwise signal the muscle to contract. The toxin thus paralyzes or weakens the injected muscle.

Botox was first approved in December 1989, to treat two eye muscle disorders (blepharospasm and strabismus) and in December 2000 to treat cervical dystonia, a neurological movement disorder causing severe neck and shoulder contractions.

In placebo-controlled, multicenter, randomized clinical trials involving a total of 405 patients with moderate to severe glabellar lines who were injected with Botox Cosmetic, data from both the investigators' and the patients' ratings of the improvement of the frown lines were evaluated. After 30 days, the great majority of investigators and patients rated frown lines as improved or nonexistent. Very few patients in the placebo group saw similar improvement.

In these studies, the severity of the glabellar lines was reduced somewhat for up to 120 days for those patients who received Botox Cosmetic. Most of the patients in the study were female, and the majority was under 50 years old. It is recommended that Botox Cosmetic be injected no more frequently than once every three months, and the lowest effective dose should be used.

The most common adverse events following injection were headache, respiratory infection, flu syndrome, blepharoptosis (droopy eyelids) and nausea. Less frequent

adverse reactions (less than 3% of patients) included pain in the face, redness at the injection site and muscle weakness. These reactions were generally temporary, but could last several months.

Because Botox Cosmetic is a prescription drug, it must be used carefully under medical supervision.

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FDA News Page | FDA Home Page

Office of Public Affairs
Web page uploaded by tg 2002-APR-15.

Exhibit 3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103000/5050

JUL 19 2004

Allergan, Incorporated
Attention: Adelbert L. Stagg, Ph.D.
Senior Director, Worldwide Regulatory Affairs
2525 Dupont Drive
Irvine, CA 92623-9534

Dear Dr. Stagg:

Your request to supplement your biologics license application for Botulinum Toxin Type A to include a new indication for primary axillary hyperhidrosis has been approved.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred.

Your supplement was submitted without studies in pediatric patients less than 11 years of age. We are waiving the pediatric study requirement for ages 11 years and below.

We acknowledge your written commitments to provide additional information on ongoing studies and to conduct postmarketing studies as described in your letter of July 7, 2004 as outlined below:

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

1. To conduct an open-label, repeated treatment, pediatric study in 130 patients, 12-16 years of age with severe axillary hyperhidrosis that is inadequately managed with topical agents. The final study protocol will be submitted by May 31, 2005. Patient enrollment will be initiated by August 30, 2005 and the last patient will be enrolled by August 30, 2006. The last patient will leave the study by August 30, 2007, and the study will be completed by October 31, 2007. The final study report will be completed by February 28, 2008 and submitted to the Agency (including SAS data and revised labeling) by May 30, 2008.

2. To conduct an open-label, three-year safety study (USA) in at least 150 patients, 17 to 64 years of age with severe primary axillary hyperhidrosis. The final study protocol was submitted on December 21, 2001. Patient enrollment has been completed. The last patient will leave the study on December 31, 2005. The study will be completed by February 28, 2006. The final study report will be completed by June 30, 2006, and submitted to the Agency (including SAS data and revised labeling, if appropriate) by September 30, 2006.

3. To conduct an open-label, three-year safety study (non-USA) in at least 150 patients, 17 to 64 years of age with persistent severe primary hyperhidrosis of the axillae. The final study protocol was submitted on May 9, 2003. Patient enrollment has been completed. The last patient will leave the study on April 30, 2007. The study will be completed by June 30, 2007. The final study report will be completed by November 30, 2007, and submitted to the Agency (including SAS data and revised labeling, if appropriate) by September 30, 2008.

4. To conduct a double-blind, placebo-controlled, repeat treatment study in 300 patients, 12 to 75 years of age with severe primary palmar hyperhidrosis that is inadequately managed with topical agents, with onset at least one year prior to study enrollment. The final study protocol will be submitted by September 30, 2005. Patient enrollment will be initiated by November 30, 2005 and the last patient will be enrolled by August 30, 2006. The last patient will leave the study by August 30, 2007, and the study will be completed by October 31, 2007. The final study report will be completed by February 28, 2008 and submitted to the Agency (including SAS data and revised labeling) by May 30, 2008.

5. To include the text from the Warning Section on Hypersensitivity Reactions in the Botox Cosmetic label at the time of next printing in July, 2004 to be made available for production to use with product manufactured starting in July, 2004 and then distributed. This label will be submitted to the Agency as a Changes Being Effected (CBE) at printing by July 31, 2004.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103000. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 103000. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted), and
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cber/gdlns/post040401.htm) for further information.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Division of Drug Marketing, Advertising and Communication (HFD-42), Center for Drug Evaluation and Research, 5600 Fishers Lane/Room 8B45, Rockville, MD 20857. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

The regulatory responsibility for review and continuing oversight for this product transferred from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research effective June 30, 2003. For further information about the transfer, please see http://www.fda.gov/cder/biologics/default.htm. Until further notice, however, all correspondence, except as provided elsewhere in this letter, should continue to be addressed to:

CBER Document Control Center
Attn: Office of Therapeutics Research and Review
Suite 200N (HFM-99)
1401 Rockville Pike
Rockville, Maryland 20852-1448

This information will be included in your biologics license application file.

Sincerely,

(b)(6)

Marc Walton, M.D., Ph.D.
Director
Division of Therapeutic Biological Internal Medicine Products
Office of Drug Evaluation VI
Center for Drug Evaluation and Research

Enclosures: Package Insert

Exhibit 4

Product Approval Information - Licensing Action

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

December 21, 2000

Submission Tracking No. (STN) 103000/1004
(Replaces Reference Number: 91-0184)

Mr. Peter A. Kresel
Allergan, Inc.
2525 Dupont Drive
P.O. Box 195
Irvine, CA 92713-9534

Dr. Mr. Kresel:

The Supplement to your License Application for Botulinum Toxin Type A (BOTOX), to include the indication of treatment of cervical dystonia, submitted under Section 351 of the Public Health Service Act, has been approved.

Under this approval, BOTOX is indicated for the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia.

We acknowledge your commitments dated December 13, 2000, and December 15, 2000, for the following postmarketing clinical study:

1. You have agreed to initiate a postmarketing study to evaluate the safety and immunogenicity of BOTOX in patients with cervical dystonia. You have made the following commitments for timeframes of conducting the study and submission to related materials to the Center for Biologics Evaluation and Research (CBER):

a. The study protocol will be finalized and submitted to CBER for review and comment by the end of January 2001.

b. The study will be initiated by the end of March, 2001.

c. A sufficient number of study subjects will be enrolled such that a minimum of 250 subjects will complete the two years of follow-up monitoring.

d. Enrollment of study subjects will be completed in approximately 3.5 years, with the last subject to be entered by the end of December 2004.

e. All study subjects will be followed until the 2-year clinical observation period for the last enrolled patient is completed in December 2006.

f. Database closure and initiation of data analysis will occur in December 2006.

g. The clinical study final report will be completed and submitted to CBER by April 2007.

h. In addition, you have agreed to include interim data analyses in the annual reports on the status of this study.

Be advised that as of April 12, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). A waiver for pediatric studies for this application is granted under 21 CFR 601.27.

This information will be placed in your biologics license application file for this product.

Changes in the manufacturing process, manufacturing facility, product testing, packaging or labeling for Botulinum Toxin Type A (BOTOX) may require the submission of a supplement to your biologics license application for review and approval prior to implementation.

It is required that adverse experience reports be submitted in accordance with the adverse events reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-120, Food and Drug Administration, 1401 Rockville Pike, MD 20852-1448.

It is required that reports of errors and accidents in manufacture be submitted in accordance with the error and accident reporting requirements for licensed biological products (21 CFR 600.14). All error and accident reports should be identified promptly according to 21 CFR 600.14 and submitted to the Director, Office of Compliance, Center for Biological Evaluation and Research, HFM-600, 1401 Rockville Pike, MD 20852-1448.

Please submit final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies

(ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and no contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biological Evaluation and Research.

Please acknowledge receipt of this letter to the Director, Division of Vaccines and Related Products Applications, HFM-475, Center for Biological Evaluation and Research.

Sincerely yours,
--- signature ---

Karen L. Goldenthal, M.D.
Director
Division of Vaccines and Related Products Applications
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

Last Updated: 1/25/2001

Back to Top Back to Index

Date created: September 25, 2003

Exhibit 5

BOTOX® COSMETIC
(Botulinum Toxin Type A) Purified Neurotoxin Complex

Manufactured by:
Allergan Pharmaceuticals Ireland
A subsidiary of: **Allergan, Inc.**
2525 Dupont Dr.
Irvine, California 92612

Description: BOTOX® COSMETIC (Botulinum Toxin Type A) Purified Neurotoxin Complex is a sterile, vacuum-dried purified botulinum toxin type A, produced from fermentation of Hall strain *Clostridium botulinum* type A grown in a medium containing casein hydrolysate, glucose and yeast extract. It is purified from the culture solution by dialysis and a series of acid precipitations to a complex consisting of the neurotoxin, and several accessory proteins. The complex is dissolved in sterile sodium chloride solution containing Albumin Human and is sterile filtered (0.2 microns) prior to filling and vacuum-drying.

One Unit of **BOTOX® COSMETIC** corresponds to the calculated median intraperitoneal lethal dose (LD_{50}) in mice. The method utilized for performing the assay is specific to Allergan's product **BOTOX® COSMETIC**. Due to specific details of this assay such as the vehicle, dilution scheme and laboratory protocols for the various mouse LD_{50} assays, Units of biological activity of **BOTOX® COSMETIC** cannot be compared to nor converted into Units of any other botulinum toxin or any toxin assessed with any other specific assay method. Therefore, differences in species sensitivities to different botulinum neurotoxin serotypes precludes extrapolation of animal-dose activity relationships to human dose estimates. The specific activity of **BOTOX® COSMETIC** is approximately 20 units/nanogram of neurotoxin protein complex.

Each vial of **BOTOX® COSMETIC** contains 100 Units (U) of *Clostridium botulinum* type A neurotoxin complex, 0.5 milligrams of Albumin Human, and 0.9 milligrams of sodium chloride in a sterile, vacuum-dried form without a preservative.

Clinical Pharmacology: BOTOX® COSMETIC blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings. When injected intramuscularly at therapeutic doses, **BOTOX® COSMETIC** produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity. In addition, the muscle may atrophy, axonal sprouting may occur, and extrajunctional acetylcholine receptors may develop. There is evidence that reinnervation of the muscle may occur, thus slowly reversing muscle denervation produced by **BOTOX® COSMETIC**.

Pharmacokinetics
Botulinum Toxin Type A is not expected to be present in the peripheral blood at measurable levels following IM injection at the recommended doses. The recommended quantities of neurotoxin administered at each treatment session are not expected to result in systemic, overt distant clinical effects, i.e. muscle weakness, in patients without other neuromuscular dysfunction. However, sub-clinical systemic effects have been shown by single-fiber electromyography after IM doses of botulinum toxins appropriate to produce clinically observable local muscle weakness. These side effects may be due to local spread of toxin from the injection site and/or misplaced injections.

Clinical studies have reported changes in clinical electromyographic parameters (i.e., jitter) in muscles distant to the site of **BOTOX®** injection. This may indicate spread of the toxin via circulation, retro- or ortho-grade axonal transport, or some action of the toxin at a third, central, or unidentified site.

Clinical Studies:

***Glabellar Lines*:**
Two phase 3 randomized, multi-center, double blind, placebo-controlled, parallel-group studies of identical design were conducted to evaluate **BOTOX® COSMETIC** for use in the temporary improvement of the appearance of moderate to severe glabellar facial lines. The studies enrolled healthy adult patients (ages 18 to 75) with glabellar lines of at least moderate severity at maximum frown. Patients were excluded if they had an infection or skin problem at the injection site, history of facial nerve palsy, marked facial asymmetry, ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin, inability to substantially lessen glabellar lines even by physically spreading them apart or had a known history of neuromuscular disorder or other disorder that could interfere with neuromuscular function. Subjects received a single treatment of intramuscular injection with either **BOTOX® COSMETIC** (N=405, combined studies) or placebo (N=132, combined studies). Injection volume was 0.1ml/injection site, for a dose/injection site in the active treatment groups of 4 Units. Patients were to be injected intramuscularly in five sites, 1 in the procerus muscle and 2 in each corrugator supercilii muscle, for a total dose in the active treatment groups of 20 Units.

The co-primary efficacy measurements were the investigator's rating of glabellar line severity at maximum frown at Day 30 post-injection and the subject's global assessment of change in appearance of glabellar lines at Day 30 post-injection. For the investigator rating, a photoguide was provided to each study center to assist in grading the severity of glabellar lines using a 4-point grading scale (0=none 1=mild 2= moderate 3=severe). A responder was defined as having a severity grade of 0 or 1.

For the global assessment of change in appearance of glabellar lines, the subject responded to the question, "How would you rate the change in the appearance of your glabellar lines compared with immediately before your most recent injection?" The ratings of responses by subjects were from +4 (complete improvement, about 100%) to -4 (very marked worsening, about 100% worse or greater). A responder was defined as having a grade of at least +2 (moderate improvement, about 50%).

A secondary efficacy endpoint was the investigator's rating of glabellar line severity at rest at Day 30 post-injection in those subjects who at baseline demonstrated a glabellar line severity score *at rest* of moderate or severe.

For the investigators' rating, the criteria for effectiveness was a 30 percentage point difference between **BOTOX® COSMETIC** and placebo treatment groups in the incidence of subjects with an investigator's rating of glabellar line severity of none or mild at maximum frown. For the subjects' rating, the criteria for effectiveness was a 25 percentage point difference between **BOTOX® COSMETIC** and placebo treatment groups in the incidence of subjects with a score of at least +2 (moderate improvement) in subject's global assessment of change in the appearance of glabellar lines.

The combined results of these two efficacy trials with the same design are presented here. There were 210 subjects (161 subjects in the **BOTOX® COSMETIC** treated group and 49 subjects in the placebo treated group) who had glabellar line severity scores at rest of moderate or severe.

The mean age was 46.0 years, with a range of 22 to 78 years. Of these, 68.2% (366/537) were ≤ 50 years of age and 31.8% (171/537) were ≥ 51 years of age and 6.0% were ≥ 65 years of age.

Most of the subjects were female, 81.9% (440/537) and Caucasian, 83.8% (450/537).

In these studies, the severity of glabellar lines was reduced for up to 120 days in the **BOTOX® COSMETIC** group compared to the placebo group as measured both by investigator rating of glabellar line severity at maximum frown and at rest, and by subject's global assessment of change in appearance of glabellar lines. By Day 7, 74% (299/405) of subjects had achieved a severity score of none or mild at maximum frown by the investigator's assessment. This increased to 80% (325/405) by the primary efficacy endpoint day of Day 30, compared to 3% of placebo-treated patients (Table 1). By Day 7, 83% (334/405) of subjects assessed moderate or better improvement in their own appearance (+2 or better). This increased to 89% (362/405) by the primary efficacy endpoint day of Day 30, compared to 7% of placebo-treated patients (Table 2). Based on resting appearance as judged by the investigator, 68% (110/161) of subjects achieved a severity score of none or mild at Day 7, and 74% (119/161) by the efficacy endpoint day of Day 30 (Table 3).

TABLE 1.
Investigator's Assessment—Responder Rates Assessed at Maximum Frown (% and Number of Subjects with Severity of None or Mild)

DAY	BOTOX® COSMETIC	PLACEBO	DIFFERENCE [a]	P-VALUE
7	73.8% 299/405	6.1% 8/132	67.8% (61.9, 73.7)	<0.001
30*	80.2% 325/405	3.0% 4/132	77.2% (72.4, 82.1)	<0.001
60	70.2% 283/403	1.5% 2/130	68.7% (63.7, 73.6)	<0.001
90	47.6% 192/403	2.3% 3/128	45.3% (39.8, 50.8)	<0.001
120	25.3% 102/403	1.6% 2/128	23.8% (19.0, 28.5)	<0.001

[a] 95% confidence intervals are shown in parentheses
* Day 30: Co-Primary Efficacy Timepoint

TABLE 2.

Subject's Assessment—Responder Rates of Appearance (% and Number of Subjects with at Least Moderate Improvement)

DAY	BOTOX® COSMETIC	PLACEBO	DIFFERENCE[a]	P-VALUE
7	82.5% 334/405	9.1% 12/132	73.4% (67.2, 79.5)	<0.001
30*	89.4% 362/405	6.8% 9/132	82.6% (77.3, 87.8)	<0.001
60	81.9% 330/403	3.8% 5/130	78.0% (73.0, 83.1)	<0.001
90	63.0% 254/403	3.1% 4/128	59.9% (54.3, 65.5)	<0.001
120	39.0% 157/403	0.8% 1/128	38.2% (33.2, 43.2)	<0.001

[a] 95% confidence intervals are shown in parentheses
* Day 30: Co-Primary Efficacy Timepoint

TABLE 3.

Investigator's Assessment—Responder Rates Assessed at Rest in Subjects with Moderate or Severe Severity Score at Baseline (% and Number of Subjects with Severity of None or Mild)

DAY	BOTOX® COSMETIC	PLACEBO	DIFFERENCE [a]	P-VALUE
7	68.3% 110/161	24.5% 12/49	43.8% (29.8, 57.9)	<0.001
30*	73.9% 119/161	20.4% 10/49	53.5% (40.3, 66.7)	<0.001
60	72.7% 117/161	24.5% 12/49	48.2% (34.3, 62.1)	<0.001
90	70.8% 114/161	34.7% 17/49	36.1% (21.1, 51.2)	<0.001
120	59.0% 95/161	34.7% 17/49	24.3% (9.0, 39.7)	0.007

[a] 95% confidence intervals are shown in parentheses
* Day 30: Secondary Endpoint

The responder rates for both co-primary efficacy variables were higher for subjects ≤ 50 years of age than for those ≥ 51 years to ≤ 65 years of age (Tables 4 and 5). Efficacy was higher for both groups compared to those subjects ≥ 65 years of age (Tables 6 and 7). In the cervical dystonia trial, there was also a consistently observed treatment-associated effect between subsets greater than and less than 65 years of age. (See Precautions: Geriatrics) There were no statistically significant between-group differences for the investigator's assessment at maximum frown for this age group. There was a statistically significant difference in favor of **BOTOX® COSMETIC** for the subject's global assessment at all time points except Day 120 ($p \leq 0.036$).

TABLE 4.
Investigator's Assessment--Responder Rates of Glabellar Line Severity by Age Distribution

Investigator's Assessment at Maximum Frown % rated 0 or 1 ≤ 50 years			Investigator's Assessment at Maximum Frown % rated 0 or 1 > 50 years		Investigator's Assessment at Maximum Frown % rated 0 or 1 > 65 years	
DAY	BOTOX® COSMETIC	Placebo	BOTOX® COSMETIC	Placebo	BOTOX® COSMETIC	Placebo
7	80.7% 226/280	5.8% 5/86	58.4% 73/125	6.5% 3/46	34.8% 8/23	11.1% 1/9
30 *	84.6% 237/280	2.3% 2/86	70.4% 88/125	4.3% 2/46	39.1% 9/23	22.2% 2/9
60	73.6% 206/280	1.2% 1/85	62.6% 77/123	2.2% 1/45	30.4% 7/23	12.5% 1/8
90	50.4% 141/280	1.2% 1/83	41.5% 51/123	4.4% 2/45	30.4% 7/23	12.5% 1/8
120	28.6% 80/280	0% 0/83	17.9% 22/123	4.4% 2/45	4.3% 1/23	12.5% 1/8

* Day 30: Co-Primary Efficacy Timepoint

TABLE 5.
Subject's Assessment--Responder Rates of Glabellar Line Severity by Age Distribution

	Subject's Assessment % +2 or better ≤ 50 years		Subject's Assessment % +2 or better > 50 years		Subject's Assessment % +2 or better > 65 years	
DAY	**BOTOX® COSMETIC**	**Placebo**	**BOTOX® COSMETIC**	**Placebo**	**BOTOX® COSMETIC**	**Placebo**
7	86.8% 243/280	7.0% 6/86	72.8% 91/125	13.0% 6/46	52.2% 12/23	11.1% 1/9
30 *	91.8% 257/280	3.5% 3/86	84.0% 105/125	13.0% 6/46	69.6% 16/23	11.1% 1/9
60	84.6% 237/280	3.5% 3/85	75.6% 93/123	4.4% 2/45	65.2% 15/23	0% 0/8
90	63.2% 177/280	2.4% 2/83	62.6% 77/123	4.4% 2/45	65.2% 15/23	0% 0/8
120	41.1% 115/280	1.2% 1/83	34.1% 42/123	0% 0/45	17.4% 4/23	0% 0/8

* Day 30: Co-Primary Efficacy Timepoint

TABLE 6.
Investigators Assessment--Responder Rates at Maximum Frown (% and Number of Subjects with Severity of None or Mild) for Subjects >65 Years of Age

DAY	BOTOX® COSMETIC N=23	PLACEBO N=9	DIFFERENCE	RELATIVE RISK	P-VALUE
7	34.8% 8/23	11.1% 1/9	23.67 (-4.62, 51.96)	3.13 (0.45, 21.58)	0.188
30 *	39.1% 9/23	22.2% 2/9	16.91 (-16.8, 50.61)	1.76 (0.47, 6.62)	0.373
60	30.4% 7/23	12.5% 1/8	17.93 (-11.7, 47.58)	2.43 (0.35, 16.85)	0.326
90	30.4% 7/23	12.5% 1/8	17.93 (-11.7, 47.58)	2.43 (0.35, 16.85	0.326
120	4.3% 1/23	12.5% 1/8	-8.15% (-32.5, 16.23)	0.35 (0.02, 4.94)	0.426

* Day 30: Co-Primary Efficacy Timepoint

TABLE 7.
Subject's Assessment– Responder Rates at Maximum Frown (% and Number of Subjects with Severity of None or Mild) for Subjects >65 Years of Age

DAY	BOTOX® COSMETIC N=23	PLACEBO N=9	DIFFERENCE	RELATIVE RISK	P-VALUE
7	52.2% 12/23	11.1% 1/9	41.06 (12.11, 70.02)	4.70 (0.71, 31.05)	0.036
30 *	69.6% 16/23	11.1% 1/9	58.45 (30.61, 86.30)	6.26 (0.97, 40.52)	0.003
60	65.2% 15/23	0% 0/8	65.22 (45.75, 84.68)	11.63 (0.77, 174.7)	0.002
90	65.2% 15/23	0% 0/8	65.22 (45.75, 84.68)	11.63 (0.77, 174.7)	0.002
120	17.4% 4/23	0% 0/8	17.39 (1.90, 32.88)	3.38 (0.20, 56.59)	0.214

* Day 30: Co-Primary Efficacy Timepoint

Exploratory analyses of subsets by patient gender suggest that both genders receive benefit, although female patients may receive somewhat greater amounts than male patients. The responder rates for both co-primary efficacy variables were higher for female subjects than for males (Tables 8 and 9).

TABLE 8.
Investigator's Assessment--Responder Rates of Glabellar Line Severity by Gender

Investigator's Assessment At Maximum Frown % rated 0 or 1 FEMALE			Investigator's Assessment At Maximum Frown % rated 0 or 1 MALE	
DAY	BOTOX® COSMETIC		BOTOX® COSMETIC	
30 *	84.7% 283/334		59.2% 42/71	
120	27.7% 92/332		14.1% 10/71	

* Day 30: Co-Primary Efficacy Timepoint

TABLE 9.
Subject's Assessment--Responder Rates of Glabellar Line Severity by Gender

Subject's Assessment % +2 or better FEMALE			Subject's Assessment % +2 or better MALE	
DAY	BOTOX® COSMETIC		BOTOX® COSMETIC	
30 *	93.1% 311/334		71.8% 51/71	
120	42.8% 142/332		21.1% 15/71	

* Day 30: Co-Primary Efficacy Timepoint

There were too few non-Caucasian patients enrolled to draw any conclusions regarding relative efficacy in racial subsets. The responder rates for both co-primary efficacy variables were slightly higher for Caucasian than for non-Caucasian subjects (Tables 10 and 11).

TABLE 10.
Investigator's Assessment--Responder Rates of Glabellar Line Severity by Race

	Investigator's Assessment At Maximum Frown % rated 0 or 1 CAUCASIAN		Investigator's Assessment At Maximum Frown % rated 0 or 1 NON-CAUCASIAN	
DAY	BOTOX® COSMETIC		BOTOX® COSMETIC	
30 *	81.2% 277/341		75.0% 48/64	
120	25.7% 87/339		23.4% 15/64	

* Day 30: Co-Primary Efficacy Timepoint

TABLE 11.
Subject's Assessment--Responder Rates of Glabellar Line Severity by Race

	Subject's Assessment % +2 or better CAUCASIAN		Subject's Assessment % +2 or better NON-CAUCASIAN	
DAY	BOTOX® COSMETIC		BOTOX® COSMETIC	
30 *	89.7% 306/341		87.5% 56/64	
120	40.1% 136/339		32.8% 21/64	

* Day 30: Co-Primary Efficacy Timepoint

Responder rates for both co-primary efficacy variables tended to be lower for subjects with a severe baseline score at maximum frown compared to subjects with a moderate baseline score (Tables 12 and 13). The proportion who had their score rated as none to mild at rest after treatment was higher in the **BOTOX® COSMETIC** treated group as compared to the placebo treated group ($p \leq 0.022$) for every time-point beginning at Day 7 through Day 120 in study 010 and through Day 90 in study 023.

TABLE 12.
Investigator's Assessment--Responder Rates of Glabellar Line Severity by Baseline Glabellar Line Severity at Maximum Frown

	Investigator's Assessment At Maximum Frown % rated 0 or 1 MODERATE		Investigator's Assessment At Maximum Frown % rated 0 or 1 SEVERE	
DAY	BOTOX® COSMETIC	Placebo	BOTOX® COSMETIC	Placebo
30 *	95.8% 159/166	1.8% 1/56	69.5% 166/239	1.4% 1/74
120	39.6% 65/164	1.8% 1/55	15.5% 37/238	1.4% 1/73

* Day 30: Co-Primary Efficacy Timepoint

TABLE 13.
Subject's Assessment--Responder Rates of Glabellar Line Severity by Baseline Glabellar Line Severity

	Subject's Assessment % +2 or better MODERATE		Subject's Assessment % +2 or better SEVERE	
DAY	BOTOX® COSMETIC	Placebo	BOTOX® COSMETIC	Placebo
30 *	94.0% 156/166	7.1% 4/56	86.2% 206/239	4.1% 3/74
120	50.6% 83/164	0% 0/55	31.0% 74/239	1.4% 1/73

* Day 30: Co-Primary Efficacy Timepoint

On completion of the efficacy trial, participants were invited to participate in a multicenter, open-label, non-comparative study to evaluate the safety of repeated treatments with **BOTOX® COSMETIC** using the same dose and procedure from the previous studies. Only patients who had a glabellar line severity rating of mild or greater at maximum frown at the time of enrollment were admitted to the open-label safety evaluation study. A total of 373 subjects (72.6%) were enrolled in this open-label study and 318 subjects completed the study. There were a total of 258 subjects who received **BOTOX® COSMETIC** in the previous trials and both injections of **BOTOX® COSMETIC** during this trial (for a total treatment time of 12 months). Of these, 239 subjects completed the 120 days of follow-up after the final injection. The open-label study was designed specifically to evaluate the safety of repeated treatments. In the open-label, repeat injection study, blepharoptosis was reported for 2.1% (8/373) of subjects in the first treatment cycle and 1.2% (4/343) of subjects in the second treatment cycle. Adverse events of any type were reported for 49.1% (183/373) of subjects.

Cosmetic Indications and Usage:

BOTOX® COSMETIC is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients ≤ 65 years of age.

Contraindications: **BOTOX® COSMETIC** is contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any ingredient in the formulation.

Warnings:

Do not exceed the recommended dosage and frequency of administration of **BOTOX® COSMETIC**. Risks resulting from administration at higher dosages are not known.

Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been rarely reported. These reactions include anaphylaxis, urticaria, soft tissue edema, and dyspnea. One fatal case of anaphylaxis for another indication has been reported in which lidocaine was used as the diluent, and consequently the causal agent cannot be reliably determined. If such a reaction occurs further injection of **BOTOX®** should be discontinued and appropriate medical therapy immediately instituted.

Pre-Existing Neuromuscular Disorders
Caution should be exercised when administering **BOTOX® COSMETIC** to individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis, or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of **BOTOX® COSMETIC**. Published medical literature has reported rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of these cases, dysphagia has lasted several months and required placement of a gastric feeding tube.

Dysphagia
Dysphagia is a commonly reported adverse event following treatment of cervical dystonia patients with all botulinum toxins. In these patients, there are reports of rare cases of dysphagia severe enough to warrant the insertion of a gastric feeding tube. There is also a case report where a patient developed aspiration pneumonia and died subsequent to the finding of dysphagia.

Cardiovascular System
There have been rare reports following administration of **BOTOX®** for other indications of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease.

Human Albumin
This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

Precautions:

General: Epinephrine should be available or other precautionary methods taken as necessary should an anaphylactic reaction occur.

The safe and effective use of **BOTOX® COSMETIC** depends upon proper storage of the product, selection of the correct dose, and proper reconstitution and administration techniques. Physicians administering **BOTOX® COSMETIC** must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures. Caution should be used when **BOTOX® COSMETIC** treatment is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle(s).

Reduced blinking from **BOTOX® COSMETIC** injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorders. In the use of **BOTOX®** for in the treatment of blepharospasm, one case of corneal perforation in an aphakic eye requiring corneal grafting has occurred because of this effect. Careful testing of corneal sensation in eyes previously operated upon, avoidance of injection into the lower lid area to avoid ectropion, and vigorous treatment of any epithelial defect should be employed. This may require protective drops, ointment, therapeutic soft contact lenses, or closure of the eye by patching or other means.

Inducing paralysis in one or more extraocular muscles may produce spatial disorientation, double vision or past pointing. Covering the affected eye may alleviate these symptoms.

Caution should be used when **BOTOX® COSMETIC** treatment is used in patients who have an inflammatory skin problem at the injection site, marked facial asymmetry, ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin or the inability to substantially lessen glabellar lines by physically spreading them apart as these patients were excluded from the Phase 3 safety and efficacy trials. As with any injection, procedure-related injury could occur. An injection could result in localized infection, pain, inflammation, tenderness, swelling, erythema, and/or bleeding/bruising. Caution should be used in patients who have bleeding disorders or are taking anticoagulants. Needle-related pain and/or anxiety may result in vasovagal responses, e.g. syncope, hypotension, etc. Care should be taken when injecting near vulnerable anatomic structures.

Injection intervals of **BOTOX® COSMETIC** should be no more frequent than every three months and should be performed using the lowest effective dose (See Adverse Reactions, Immunogenicity).

Information for Patients:
Patients or caregivers should be advised to seek immediate medical attention if swallowing, speech or respiratory disorders arise.

Drug Interactions:
Co-administration of **BOTOX® COSMETIC** and aminoglycosides[1] or other agents interfering with neuromuscular transmission (e.g., curare-like nondepolarizing blockers, lincosamides, polymyxins, quinidine, magnesium sulfate, anticholinesterases, succinylcholine chloride) should only be performed with caution as the effect of the toxin may be potentiated.

The effect of administering different botulinum neurotoxin serotypes at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

Pregnancy: Pregnancy Category C
Administration of **BOTOX® COSMETIC** is not recommended during pregnancy. There are no adequate and well-controlled studies of **BOTOX® COSMETIC** in pregnant women. When pregnant mice and rats were injected intramuscularly during the period of organogenesis, the developmental NOEL (No Observed Effect Level) of **BOTOX® COSMETIC** was 4 U/kg. Higher doses (8 or 16 U/kg) were associated with reductions in fetal body weights and/or delayed ossification.

In a range finding study in rabbits, daily injection of 0.125 U/kg/day (days 6 to 18 of gestation) and 2 U/kg (days 6 and 13 of gestation) produced severe maternal toxicity, abortions and/or fetal malformations. Higher doses resulted in death of the dams. The rabbit appears to be a very sensitive species to **BOTOX® COSMETIC**.

If the patient becomes pregnant after the administration of this drug, the patient should be apprised of the potential risks, including abortion or fetal malformations that have been observed in rabbits.

***Carcinogenesis, Mutagenesis, Impairment of fertility*:**
Long term studies in animals have not been performed to evaluate carcinogenic potential of **BOTOX® COSMETIC**.

The reproductive NOEL following intramuscular injection of 0, 4, 8, and 16 U/kg was 4 U/kg in male rats and 8 U/kg in female rats. Higher doses were associated with dose-dependent reductions in fertility in male rats (where limb weakness resulted in the inability to mate), and testicular atrophy or an altered estrous cycle in female rats. There were no adverse effects on the viability of the embryos.

Nursing mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **BOTOX® COSMETIC** is administered to a nursing woman.

Pediatric use: Use of **BOTOX® COSMETIC** is not recommended in children.

Geriatric use: Clinical studies of **BOTOX® COSMETIC** did not include sufficient numbers of subjects aged 65 and over to determine statistically whether they respond differently from younger subjects. However, in the two identical phase 3 randomized 3:1, multi-center, double blind, placebo-controlled, parallel-group efficacy studies, the responder rates for both co-primary efficacy variables were higher for subjects ≤ 50 years of age compared to those subjects ≥ 65 years of age. Analysis based on a combined data set showed that, for the investigator's assessment endpoint of subjects aged 65 and over at Day 30, 39% (9/23) of subjects were responders compared to 22% (2/9) in the placebo group. This difference is neither statistically different (p= 0.228) nor exceeds the pre-specified 30-percentage-point difference required by the definition of clinically significant. There were no statistically significant between-group differences for the investigator's assessment at maximum frown for this age group. There was a statistically significant difference in favor of **BOTOX® COSMETIC** for the subject's global assessment at all time points ($p \leq 0.036$) except Day 120 ($p = 0.214$). (See Clinical Trials Section)

There were too few patients over the age of 75 to allow any meaningful comparisons. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased cardiac function and of concomitant disease or other drug therapy.

Adverse Reactions:

General:

The most serious adverse events reported for other indications studied include rare spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility, after treatment with botulinum toxin. There have also been rare reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease. (See Warnings) In addition, there have been rare reports of seizures or convulsions, mostly in patients who are predisposed to experiencing these events. The exact relationship of these events to the botulinum toxin injection has not been established. Additionally, a report of acute angle closure glaucoma one day after receiving an injection of botulinum toxin for blepharospasm was received, with recovery four months later after laser iridotomy and trabeculectomy. Focal facial paralysis, syncope and exacerbation of myasthenia gravis have also been reported after treatment of blepharospasm.

In general, adverse events occur within the first week following injection of **BOTOX® COSMETIC** and while generally transient may have a duration of several months or, in rare cases, longer.

Glabellar Lines:

In clinical trials of **BOTOX® COSMETIC** the most frequently reported adverse events following injection of **BOTOX® COSMETIC** were headache, respiratory infection, flu syndrome, blepharoptosis and nausea.

Less frequently occurring (<3%) adverse reactions included pain in the face, erythema at the injection site and muscle weakness. While local weakness of the injected muscle(s) is representative of the expected pharmacological action of botulinum toxin, weakness of adjacent muscles may occur as a result of the spread of toxin. These events are thought to be associated with the injection and occurred within the first week. The events were generally transient but may last several months or, in rare cases, longer.

The data described in Table 14 reflect exposure to **BOTOX® COSMETIC** in 405 subjects aged 18 to 75 who were evaluated in the randomized, placebo-controlled clinical studies to assess the use of **BOTOX® COSMETIC** in the improvement of the appearance of glabellar lines (See Clinical Studies). Adverse events of any cause were reported for 43.7% of the **BOTOX® COSMETIC** treated subjects and 41.5% of the placebo treated subjects. The incidence of blepharoptosis was higher in the **BOTOX® COSMETIC** treated arm than in placebo (3.2% vs. 0%, p-value = 0.045).

In the open-label, repeat injection study, blepharoptosis was reported for 2.1% (8/373) of subjects in the first treatment cycle and 1.2% (4/343) of subjects in the second treatment cycle. Adverse events of any type were reported for 49.1% (183/373) of subjects overall. The most frequently reported of these adverse events in the open-label study included respiratory infection, headache, flu syndrome, blepharoptosis, pain and nausea.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not be predictive of rates observed in practice.

TABLE 14.
Randomized Double Blind Studies: Rates of Adverse Events Reported by >2 or more Subjects in the BOTOX® COSMETIC Group, by Treatment Group.

Adverse Event (in order of decreasing frequency for BOTOX® COSMETIC)	BOTOX® COSMETIC (N=405)	Placebo (N= 130)
Overall	177 (43.7%)	54 (41.5%)
Body as a Whole		
Headache	54 (13.3%)	23 (17.7%)
Pain in Face	9 (2.2%)	1 (0.8%)
Flu Syndrome	8 (2.0%)	2 (1.5%)
Pain at Injection Site	7 (1.7%)	1 (0.8%)
Edema at Injection Site	6 (1.5%)	3 (2.3%)
Pain in back	4 (1.0%)	3 (2.3%)
Injury accidental	3 (0.7%)	1 (0.8%)
Respiratory System		
Infection	14 (3.5%)	5 (3.8%)
Bronchitis	6 (1.5%)	1 (0.8%)
Sinusitis	6 (1.5%)	1 (0.8%)
Pharyngitis	5 (1.2%)	2 (1.5%)
Dyspnea	3 (0.7%)	0 (0.0%)
Infection sinus	3 (0.7%)	2 (1.5%)
Laryngitis	3 (0.7%)	0 (0.0%)
Rhinitis	3 (0.7%)	2 (1.5%)
Skin and Appendages		
Erythema	7 (1.7%)	2 (1.5%)
Skin Tightness	4 (1.0%)	0 (0.0%)
Irritation Skin	3 (0.7%)	0 (0.0%)
Digestive System		
Nausea	12 (3.0%)	3 (2.3%)
Dyspepsia	4 (1.0%)	0 (0.0%)
Tooth Disorder	4 (1.0%)	0 (0.0%)
Liver Function Abnormal	3 (0.7%)	2 (1.5%)
Special Senses		
Blepharoptosis	13 (3.2%)	0 (0.0%)
Nervous System		
Dizziness	5 (1.2%)	2 (1.5%)
Paresthesia	4 (1.0%)	1 (0.8%)
Anxiety	3 (0.7%)	0 (0.0%)
Twitch	3 (0.7%)	0 (0.0%)
Musculoskeletal System		
Muscle Weakness	8 (2.0%)	0 (0.0%)
Urogenital System		
Infection Urinary Tract	4 (1.0%)	1 (0.8%)
Hemic and Lymphatic System		
Ecchymosis	7 (1.7%)	3 (2.3%)
Cardiovascular		
Hypertension	4 (1.0%)	0 (0.0%)

In published literature of the use of botulinum toxin type A for facial lines, there has been a single reported incident of diplopia, which resolved completely in three weeks. Transient ptosis, the most frequently reported complication, has been reported in the literature in approximately 5% of patients.

Immunogenicity:

Treatment with **BOTOX® COSMETIC** for cosmetic purposes may result in the formation of antibodies that may reduce the effectiveness of subsequent treatments with **BOTOX® COSMETIC** for glabellar lines or **BOTOX®** for other indications. Formation of neutralizing antibodies to botulinum toxin type A may reduce the effectiveness of **BOTOX® COSMETIC** treatment of the appearance of glabellar lines and the effectiveness of **BOTOX®** in the treatment of other clinical indications such as cervical dystonia, blepharospasm and strabismus by inactivating the biological activity of the toxin. The rate of formation of neutralizing antibodies in patients receiving **BOTOX® COSMETIC** has not been well studied.

The critical factors for neutralizing antibody formation have not been well characterized. The results from some studies of the use of **BOTOX®** in the treatment of other clinical indications suggest that **BOTOX®** injections at more frequent intervals or at higher doses may lead to greater incidence of antibody formation. The potential for antibody formation may be minimized by injecting the lowest effective dose given at the longest feasible intervals between injections.

Passive Adverse Event Surveillance

The following adverse reactions have been identified since the drug has been marketed: allergic reaction; brachial plexopathy; flu-like symptoms such as chest discomfort, fever, malaise, myalgia, and sweating; focal facial paralysis; gastrointestinal disturbances including abdominal pain, diarrhea, loss of appetite, nausea, and vomiting; headache; pruritus; and skin rash (including erythema multiforme, psoriasiform eruption, and urticaria). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to botulinum toxin.

Between January 1, 1990 and December 2003, there have been spontaneous reports of serious adverse events documented as being related to the reported cosmetic use of **BOTOX®** or **BOTOX® COSMETIC**, including syncope, anaphylactic reaction, myasthenia gravis, decreased hearing, ear noise and localized numbness, blurred vision and retinal vein occlusion, glaucoma, and vertigo with nystagmus.

Reporting Adverse Events

Adverse events following use of **BOTOX® COSMETIC** should be reported to the Pharmacovigilance Department, Allergan Inc. (1-800-433-8871). Adverse events may also be reported to the U. S. Department of Health and Human Services (DHHS) Adverse Event Reporting System. Report forms and reporting requirement information can be obtained from Adverse Event Reporting System (AERS) through a toll free number 1-800-822-7967.

Overdosage:

Signs and symptoms of overdose are not apparent immediately post injection. Should accidental injection or oral ingestion occur, the person should be medically supervised for up to several weeks for signs or symptoms of systemic weakness or muscle paralysis.

An antitoxin is available in the event of immediate knowledge of an overdose or misinjection. In the event of an overdose or injection into the wrong muscle, immediately contact Allergan for additional information at (800) 433-8871 from 8:00 a.m. to 4:00 p.m. Pacific Time, or at (714) 246-5954 for a recorded message at other times. The antitoxin will not reverse any botulinum toxin induced muscle weakness effects already apparent by the time of antitoxin administration.

Dosage and Administration:

For Intramuscular Injection Only

BOTOX® COSMETIC is to be reconstituted only with 0.9% sterile, non-preserved saline (100 Units in 2.5 mL saline) prior to intramuscular injection. The resulting formulation will be 4.0 Units per 0.1 mL and a total treatment dose of 20 Units in 0.5 mL. The duration of activity of **BOTOX® COSMETIC** for glabellar lines is approximately 3-4 months. The safety and effectiveness of more frequent dosing with **BOTOX® COSMETIC** has not been clinically evaluated and is not recommended.

Reconstituted **BOTOX® COSMETIC** should be clear, colorless and free of particulate matter.

BOTOX® COSMETIC is supplied as a single patient use vial. The product and diluent do not contain a preservative. Once opened and reconstituted it should be stored in a refrigerator (2° to 8°C) and used within four hours. Discard any remaining solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not freeze reconstituted **BOTOX® COSMETIC**.

The method utilized for performing the potency assay is specific to Allergan's Botulinum Toxin Type A. Due to specific details of this assay such as the vehicle, dilution scheme and laboratory protocols for the various potency assays, Units of biological activity of Botulinum Toxin Type A cannot be compared to nor converted into Units of any other botulinum toxin or any toxin assessed with any other specific assay method. Therefore, differences in species sensitivities to different botulinum neurotoxin serotypes precludes extrapolation of animal dose-activity relationships to human dose relationships.

Dilution Technique:

Using a 21-gauge needle and an appropriately sized syringe draw up a total of 2.5 mL of 0.9% sterile saline without a preservative. Insert the needle at a 45° angle and slowly inject into the **BOTOX® COSMETIC** vial. Discard the vial if a vacuum does not pull the diluent into the vial. Gently rotate the vial and record the date and time of reconstitution on the space on the label.

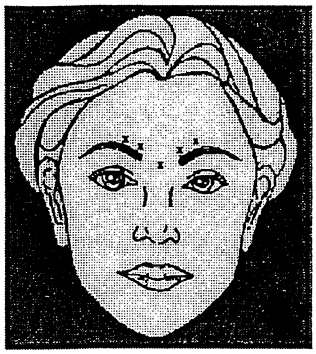
Draw at least 0.5 mL of the properly reconstituted toxin into the sterile syringe, preferably a tuberculin syringe and expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach a 30-gauge needle. Confirm the patency of the needle.

Injection Technique:
Glabellar facial lines arise from the activity of the corrugator and orbicularis oculi muscles. These muscles move the brow medially, and the procerus and depressor supercilii pull the brow inferiorly. This creates a frown or "furrowed brow". The location, size, and use of the muscles vary markedly among individuals. Lines induced by facial expression occur perpendicular to the direction of action of contracting facial muscles. An effective dose for facial lines is determined by gross observation of the patient's ability to activate the superficial muscles injected.
In order to reduce the complication of ptosis the following steps should be taken:

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Lateral corrugator injections should be placed at least 1 centimeter above the bony supraorbital ridge.
- Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- Do not inject toxin closer than 1 cm above the central eyebrow.

Using a 30-gauge needle, inject a dose of 0.1 mL into each of 5 sites, 2 in each corrugator muscle and 1 in the procerus muscle for a total dose of 20 Units. Typically the initial doses of reconstituted **BOTOX®**

COSMETIC induce chemical denervation of the injected muscles one to two days after injection, increasing in intensity during the first week.



How Supplied: BOTOX® COSMETIC is supplied in a single patient use vial. Each vial contains 100 Units of vacuum-dried *Clostridium botulinum* type A neurotoxin complex. NDC 0023-9232-01.

Vials of **BOTOX® COSMETIC** have a holographic film on the vial label that contains the name "Allergan" within horizontal lines of rainbow color. In order to see the hologram, rotate the vial back and forth between your fingers under a desk lamp or fluorescent light source. (Note: the holographic film on the label is absent in the date/batch area.) If you do not see the lines of rainbow color or the name "Allergan", do not use the product and contact Allergan for additional information at (800) 890-4345 from 8:00 a.m. to 4:00 p.m. Pacific time.

Rx Only

Single use vial.

Storage:
Unopened vials of **BOTOX® COSMETIC** should be stored in a refrigerator (2° to 8°C) for up to 24 months. Administer **BOTOX® COSMETIC** within 4 hours of reconstitution; during this period reconstituted **BOTOX® COSMETIC** should be stored in a refrigerator (2° to 8°C). Reconstituted **BOTOX® COSMETIC** should be clear, colorless and free of particulate matter. Do not use after the expiration date on the vial.
All vials, including expired vials, or equipment used with the drug should be disposed of carefully as is done with all medical waste.

® Marks owned by Allergan., Inc.

Revised July 2004

Manufactured by: Allergan Pharmaceuticals Ireland
a subsidiary of: Allergan, Inc., 2525 Dupont Dr., Irvine, CA 92612

Reference: Wang YC, Burr DH, Korthals GJ, Sugiyama H. Acute toxicity of aminoglycoside antibiotics as an aid in detecting botulism. Appl Environ Microbiol 1984; 48:951-955.

§ 11340.6. Petition requesting adoption, amendment, or repeal of regulation; Contents

Except where the right to petition for adoption of a regulation is restricted by statute to a designated group or where the form of procedure for such a petition is otherwise prescribed by statute, any interested person may petition a state agency requesting the adoption, amendment, or repeal of a regulation as provided in Article 5 (commencing with Section 11346). This petition shall state the following clearly and concisely:

(a) The substance or nature of the regulation, amendment, or repeal requested.

(b) The reason for the request.

(c) Reference to the authority of the state agency to take the action requested.

§ 11340.7. Procedure upon petition requesting adoption, amendment or repeal of regulation

(a) Upon receipt of a petition requesting the adoption, amendment, or repeal of a regulation pursuant to Article 5 (commencing with Section 11346), a state agency shall notify the petitioner in writing of the receipt and shall within 30 days deny the petition indicating why the agency has reached its decision on the merits of the petition in writing or schedule the matter for public hearing in accordance with the notice and hearing requirements of that article.

(b) A state agency may grant or deny the petition in part, and may grant any other relief or take any other action as it may determine to be warranted by the petition and shall notify the petitioner in writing of this action.

(c) Any interested person may request a reconsideration of any part or all of a decision of any agency on any petition submitted. The request shall be submitted in accordance with Section 11340.6 and include the reason or reasons why an agency should reconsider its previous decision no later than 60 days after the date of the decision involved. The agency's reconsideration of any matter relating to a petition shall be subject to subdivision (a).

(d) Any decision of a state agency denying in whole or in part or granting in whole or in part a petition requesting the adoption, amendment, or repeal of a regulation pursuant to Article 5 (commencing with Section 11346) shall be in writing and shall be transmitted to the Office of Administrative Law for publication in the California Regulatory Notice Register at the earliest practicable date. The decision shall identify the agency, the party submitting the petition, the provisions of the California Code of Regulations requested to be affected, reference to authority to take the action requested, the reasons supporting the agency determination, an agency contact person, and the right of interested persons to obtain a copy of the petition from the agency.

State of California

BOARD OF EQUALIZATION

SALES AND USE TAX REGULATIONS

REGULATION 1591. MEDICINES AND MEDICAL DEVICES.

Reference: Sections 6006 and 6369 Revenue and Taxation Code.

(a) DEFINITIONS.

(1) ADMINISTER. "Administer" means the direct application of a drug or device to the body of a patient or research subject by injection, inhalation, ingestion, or other means.

(2) DISPENSE. "Dispense" means the furnishing of drugs or devices upon a prescription from a physician, dentist, optometrist, or podiatrist. Dispense also means and refers to the furnishing of drugs or devices directly to a patient by a physician, dentist, optometrist, or podiatrist acting within the scope of his or her practice.

(3) FURNISH. "Furnish" means to supply by any means, by sale or otherwise.

(4) HEALTH FACILITY. "Health Facility" as used herein has the meaning ascribed to the term in section 1250 of the Health and Safety Code, which provides that:

"As used in this chapter 'health facility' means any facility, place or building that is organized, maintained, and operated for the diagnosis, care, prevention, and treatment of human illness, physical or mental, including convalescence and rehabilitation and including care during and after pregnancy, or for any one or more of these purposes, for one or more persons, to which the persons are admitted for a 24-hour stay or longer...."

(5) PHARMACIST. "Pharmacist" means a person to whom a license has been issued by the California State Board of Pharmacy, under the provisions of section 4200 of the Business and Professions Code, except as specifically provided otherwise in Chapter 9 of the Pharmacy Law."

(6) PHARMACY. "Pharmacy" means an area, place, or premises licensed by the California State Board of Pharmacy in which the profession of pharmacy is practiced and where prescriptions are compounded. Pharmacy includes, but is not limited to, any area, place, or premises described in a license issued by the California State Board of Pharmacy wherein controlled substances, dangerous drugs, or dangerous devices are stored, possessed, prepared, manufactured, derived, compounded, or repackaged, and from which the controlled substances, dangerous drugs, or dangerous devices are furnished, sold, or dispensed at retail. Pharmacy shall not include any area specifically excluded by paragraph (b) of section 4037 of the Business and Professions Code.

(7) PRESCRIPTION. "Prescription" means an oral, written, or electronic transmission order that is issued by a physician, dentist, optometrist, or podiatrist licensed in this state *and* given individually for the person or persons for whom ordered. The order must include all of the following:

(A) The name or names and address of the patient or patients.

(B) The name and quantity of the drug or device prescribed and the directions for use.

(C) The date of issue.

(D) Either rubber stamped, typed, or printed by hand or typeset, the name, address, and telephone number of the prescriber, his or her license classification, and his or her federal registry number, if a controlled substance is prescribed.

(E) A legible, clear notice of the conditions for which the drug is being prescribed, if requested by the patient or patients.

(F) If in writing, signed by the prescriber issuing the order.

(8) PHYSICIANS, DENTISTS, OPTOMETRISTS, AND PODIATRISTS. "Physicians," "dentists," "optometrists," and "podiatrists" are persons authorized by a currently valid and unrevoked license to practice their respective

professions in this state. "Physician" means and includes any person holding a valid and unrevoked physician's and surgeon's certificate or certificate to practice medicine and surgery, issued by the Medical Board of California or the Osteopathic Medical Board of California and includes an unlicensed person lawfully practicing medicine pursuant to section 2065 of the Business and Professions Code, when acting within the scope of that section.

(9) MEDICINES. "Medicines" means any substance or preparation intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease and which is commonly recognized as a substance or preparation intended for that use. The term medicines also includes certain articles, devices, and appliances as described in subdivision (b) of this regulation.

(b) "MEDICINES." The term "medicines" means and includes the following items:

(1) PREPARATIONS AND SIMILAR SUBSTANCES. Preparations and similar substances intended for use by external or internal application to the human body in the diagnosis, cure, mitigation, treatment or prevention of disease and which are commonly recognized as a substance or preparation intended for such use qualify as medicines. Tax does not apply to the sale or use of such medicines sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

"Preparations and similar substances" include, but are not limited to, drugs such as penicillin, and other antibiotics, "dangerous drugs" (drugs that require dispensing only on prescription); alcohol (70% solution) and isopropyl; aspirin; baby lotion, oil, and powder; enema preparations; hydrogen peroxide; lubricating jelly; medicated skin creams; oral contraceptives; measles and other types of vaccines; topical creams and ointments; and sterile nonpyrogenic distilled water. Preparations and similar substances applied to the human body in the diagnosis, cure, mitigation, treatment, or prevention of disease qualify as medicines. "Preparations and similar substances" also include Total Parenteral Nutrition (also called TPN), Intradialytic Parenteral Nutrition (also called IDPN), and food provided by way of enteral feeding, except when the TPN, IDPN, or food provided by enteral feeding qualifies as a meal under Regulation 1503. For purposes of this regulation, TPN, IDPN, and enteral feeding are means of providing complete nutrition to the patient; TPN and IDPN are provided in the form of a collection of glucose, amino acids, vitamins, minerals, and lipids, TPN being administered intravenously to a patient who is unable to digest food through the gastrointestinal tract and IDPN being administered to hemodialysis patients as an integral part of the hemodialysis treatment; enteral feeding is the feeding of the patient directly into the gastrointestinal tract.

2) PERMANENTLY IMPLANTED ARTICLES. Articles permanently implanted in the human body to assist the functioning of, as distinguished from replacing all or any part of, any natural organ, artery, vein or limb and which remain or dissolve in the body qualify as medicines. An article is considered to be permanently implanted if its removal is not otherwise anticipated. Tax does not apply to the sale or use of articles permanently implanted in the human body to assist the functioning of any natural organ, artery, vein or limb and which remain or dissolve in the body when such articles are sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

Permanently implanted articles include, but are not limited to, permanently implanted artificial sphincters; bone screws and bone pins, dental implant systems including dental bone screws and abutments; permanently implanted catheters; permanently implanted hydrocephalus devices and their implanted pressure regulating components; implanted defibrillators and implanted leads; pacemakers; tendon implants; testicular gel implants; and ear implants. Sutures are also included whether or not they are permanently implanted. A non-returnable, nonreusable needle fused or prethreaded to a suture is regarded as part of the suture.

Implantable articles that do not qualify as "permanently" implanted medicines include, but are not limited to, Chemoport implantable fluid systems; Port-a-Cath systems used for drug infusion purposes; disposable urethral catheters; temporary myocardial pacing leads used during surgery and recovery; and defibrillator programmer and high voltage stimulator used with an implanted defibrillator. The sale or use of these items is subject to tax.

(3) ARTIFICIAL LIMBS AND EYES. Artificial limbs and eyes, or their replacement parts, including stump socks and stockings worn with artificial legs and intraocular lenses for human beings, qualify as medicines as provided by Revenue and Taxation Code section 6369 (c)(5). Tax does not apply to the sale or use of these items when sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

(4) ORTHOTIC DEVICES. Orthotic devices and their replacement parts, other than orthodontic devices, designed to be worn on the person of the user as a brace, support or correction for the body structure are medicines

as provided under Revenue and Taxation Code section 6369(c)(3). The sale or use of orthotic devices and their replacement parts is not subject to tax when sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6). Orthotic devices and their replacement parts do not need to be furnished by a pharmacist, within the meaning of subdivision (d)(1), to be considered dispensed on prescription provided the devices are furnished pursuant to a written order of a physician or podiatrist. For the purposes of this regulation, orthotic devices furnished pursuant to a written order of a physician or podiatrist by, but not limited to, medical device retailers, clinics, physical therapists, device suppliers, intermediate care facilities, or other such persons, are deemed to be dispensed on prescription within the meaning of subdivision (d)(1).

Orthotic devices worn on the body of the person include, but are not limited to, abdominal binders and supports, ace bandages, ankle braces, anti-embolism stockings, athletic supporters (only for patients recovering from rectal or genital surgery), casts and cast components, cervical supports, neck collars, cervical traction devices, clavicular splints, post-surgical corsets, elbow supports, head halters, pelvic traction devices, post-operative knee immobilizers and braces, legging orthoses, rib belts and immobilizers, rupture holders, sacral belts, sacro-lumbar back braces, shoulder immobilizers, slings, stump shrinkers, sternum supports, support hose (and garter belts used to hold them in place), thumb and finger splints, trusses, and wrist and arm braces. All of the above must be worn on the body of the person and act as a brace, support or correction for body structure to qualify as a medicine. If any part of the orthotic device is not worn on the person, the device is not a medicine for the purposes of this regulation.

Orthopedic shoes and supportive devices for the foot do not qualify as medicines unless they are an integral part of a leg brace or artificial leg or are custom-made biomechanical foot orthoses. "Custom-made biomechanical foot orthosis" means a device that is made on a positive model of the individual patient's foot. The model may be individually constructed from suitable model material such as plaster of paris, stone, or wax, and may be manually constructed or fabricated using electronic technology.

"Custom-made biomechanical foot orthosis" do not include:

(A) any pre-made or pre-molded foot orthosis or shoe insert even if it has been modified or customized for an individual patient by the practitioner regardless of the method of modification;

(B) any foot orthosis fabricated directly on the patient's foot regardless of the method and materials used and regardless of its individual character; or

(C) any foot orthosis fabricated inside of the patient's shoe regardless of the method of manufacture and materials used and regardless of its individual character.

(5) PROSTHETIC DEVICES. Prosthetic devices and their replacements parts designed to be worn on or in the patient to replace or assist the functioning of a natural part of the human body are medicines as provided under Revenue and Taxation Code section 6369(c)(4). The sale or use of prosthetic devices and their replacement parts is not subject to tax when sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6). Prosthetic devices and their replacement parts do not need to be furnished by a pharmacist, within the meaning of subdivision (d)(1), to be considered dispensed on prescription provided the devices are furnished pursuant to a written order of a physician or podiatrist. For the purposes of this regulation, prosthetic devices furnished pursuant to a written order of a physician or podiatrist by, but not limited to, medical device retailers, clinics, physical therapists, device suppliers, intermediate care facilities, or other such persons are deemed to be dispensed on prescription within the meaning of subdivision (d)(1). For purposes of this regulation only, prosthetic devices include bags and tubing, as well as filters, locks, tape, clamps, and connectors which are integral to the tubing, each of which is used to dispense enteral feeding to the patient, including: gastrostomy tubes (also called G tubes) which are used to deliver the nutrition directly into the stomach; jejunostomy tubes (also called J tubes) which are used to deliver the nutrition directly into the intestinal tract; and nasogastric tubes (also called NG tubes) which are used to deliver the nutrition directly through the nasal passage to the stomach. For purposes of this regulation only, prosthetic devices also include needles, syringes, cannulas, bags, and tubing, as well as filters, locks, tape, clamps, and connectors which are integral to the tubing, each of which is used to dispense TPN or IDPN to the patient, provided each of these items is used primarily to dispense the TPN or IDPN.

Prosthetic devices that are considered medicines when worn on or in the patient include, but are not limited to, acetabular cups, atrial valves, breast tissue expanders and tissue expanders, cervical cuff, dacron grafts, heart valves, orbital implant, nerve cups, rhinoplasty prosthesis, neuromuscular electrical stimulators, transcutaneous nerve stimulators, urinary incontinent devices, and wigs and hairpieces prescribed by a physician or podiatrist.

Prosthetic devices that do not qualify as "medicines," include, but are not limited to, air compression pumps and pneumatic garments; noninvasive, temporary pace makers; and vacuum/constriction devices used to treat male impotency; auditory, ophthalmic and ocular devices or appliances; and dental prosthetic devices and materials such as dentures, removable or fixed bridges, crowns, caps, inlays, artificial teeth, and other dental prosthetic materials and devices. Sales of such items are subject to tax in the same manner as any other sale of tangible personal property.

(6) DRUG INFUSION DEVICES. Programmable drug infusion devices worn on or implanted in the human body which automatically cause the infusion of measured quantities of a drug on an intermittent or continuous basis at variable dose rates and at high or low fluid volume into the body of the wearer of the device qualify as medicines under Revenue and Taxation Code section 6369(c)(6). The sale or use of the qualifying infusion device is not subject to tax when the device is sold or furnished under one of the conditions provided in subdivision (d)(1) through (d)(6).

(c) EXCLUSIONS FROM THE DEFINITION OF "MEDICINES."

Except as otherwise provided in subdivision (b), the following items are specifically excluded from the definition of medicines:. Sales of these items are subject to tax in the same manner as any other sale of tangible personal property.

(1) Orthodontic, prosthetic (except as described in subdivision (b)(6)), auditory, ophthalmic or ocular devices or appliances.

(2) Articles which are in the nature of splints, bandages, pads, compresses, supports, dressings, instruments, apparatus, contrivances, appliances, devices or other mechanical, electronic, optical or physical equipment or article or the component parts and accessories thereof. "Medicines" does not include arch supports, cervical pillows, exercise weights (boots or belts), hospital beds, orthopedic shoes and supportive devices (unless an integral part of a leg brace or artificial leg), plastazote inserts, plastazote shoes, plastic shoes (custom or ready-made), sacro-ease seats, shoe modifications, spenco inserts, traction units (other than those fully worn on the patient), thermophore pads, or foot orthoses.

(3) Any alcoholic beverage the manufacture, sale, purchase, possession or transportation of which is licensed and regulated by the Alcoholic Beverage Control Act (Division 9, commencing with section 23000, of the Business and Professions Code).

(d) APPLICATION OF TAX—IN GENERAL.

Tax applies to retail sales, including over-the-counter sales of drugs and medicines, and other tangible personal property by pharmacists and others. However, tax does not apply to the sale or use of medicines when sold or furnished under one of the following conditions:

(1) prescribed for the treatment of a human being by a person authorized to prescribe the medicines, and dispensed on prescription filled by a pharmacist in accordance with law, or

(2) furnished by a licensed physician, dentist or podiatrist to his or her own patient for treatment of the patient, or

(3) furnished by a health facility for treatment of any person pursuant to the order of a licensed physician, dentist or podiatrist, or

(4) sold to a licensed physician, dentist, podiatrist or health facility for the treatment of a human being, or

(5) sold to this state or any political subdivision or municipal corporation thereof, for use in the treatment of a human being; or furnished for the treatment of a human being by a medical facility or clinic maintained by this state or any political subdivision or municipal corporation thereof, or

(6) effective January 1, 1995, furnished by a pharmaceutical manufacturer or distributor without charge to a licensed physician, surgeon, dentist, podiatrist, or health facility for the treatment of a human being, or to an institution of higher education for instruction or research. Such medicine must be of a type that can be dispensed only: (a) for the treatment of a human being, and (b) pursuant to prescriptions issued by persons authorized to prescribe medicines. The exemption provided by this subdivision applies to the constituent elements and ingredients used to produce the medicines and to the tangible personal property used to package such medicines.

(e) SPECIFIC TAX APPLICATIONS.

(1) PRESCRIPTIONS. No person other than a licensed physician, dentist, optometrist or podiatrist is authorized to prescribe or write a prescription for the treatment of a human being. Tax does not apply to the sale or use of medicines prescribed by a licensed physician, dentist, optometrist, or podiatrist for the treatment of a human being and dispensed on prescription filled by a pharmacist.

(2) LICENSED PHYSICIAN, DENTIST OR PODIATRIST. Tax does not apply to a specific charge made by a licensed physician, dentist or podiatrist to his or her own patient for medicines furnished for the treatment of the patient. Tax also does not apply to sales of medicines to licensed physicians, dentists or podiatrists for the treatment of a human being regardless of whether the licensed physician, dentist or podiatrist makes a specific charge to his or her patient for the medicines furnished.

(3) HEALTH FACILITY Tax does not apply to sales of medicines by a health facility (as defined in suddivision (a)(4)) for the treatment of any person pursuant to the order of a licensed physician, dentist or podiatrist. Tax does not apply to sales of medicines to a health facility for the treatment of a human being regardless of whether or not a specific charge is made for the medicines.

(4) PHARMACEUTICAL MANUFACTURER OR DISTRIBUTOR. Tax does not apply to the storage, use or consumption of medicines furnished by a pharmaceutical manufacturer or distributor without charge to a licensed physician, surgeon, dentist, podiatrist, or health facility for the treatment of a human being or furnished without charge to an institution of higher education for instruction or research provided the medicines furnished are of a type that can be dispensed only (1) on prescription by persons authorized to prescribe and (2) for the treatment of a human being. The exemption from tax includes the costs of the materials used to package the "sample" medicines, such as bottles, boxes, blister packs, patches impregnated with medicines, or pre-filled syringes, and the elements and ingredients used to produce the "samples" whether or not such items are purchased under a resale certificate in this state or outside this state. When a pre-filled syringe or other such delivery device is used to package and contain a sample medicine (i.e., pre-filled with the medicine) as well as to inject or otherwise administer the medicine to the patient, the exemption from tax will not be lost due to the fact that the device is used for a dual purpose. However, the use of empty syringes or other such delivery devices, furnished to the licensed physician separately or included in the packages with the medicines, is subject to tax.

This exemption applies in the same manner to the use of clinical trial medicines during the United States Food and Drug Administration's drug development and approval process. "Clinical trial medicines" are substances or preparations approved as "Investigational New Drugs" by the United States Food and Drug Administration intended for treatment of, and application to, the human body, which are furnished by a pharmaceutical developer, manufacturer, or distributor to a licensed physician and subsequently dispensed, furnished, or administered pursuant to the order of the licensed physician. "Clinical trial medicines" do not include placebos. Placebos are not used for the treatment of a human being and, as such, do not qualify for the exemption provided under this subdivision. Thus, the use of placebos is subject to tax.

(5) ANTIMICROBIAL AGENTS USED BY HOSPITAL PERSONNEL. Tax does not apply to the sale or use of substances or preparations, such as antiseptic cleansers or scrubs, when such substances or preparations qualify as medicines and are used by hospital personnel on the patient or by hospital personnel on their own bodies to benefit the patient, and which constitute a critical component of the patient's treatment. Qualifying medicines used on the bodies of hospital personnel include antimicrobial agents used for preoperative scrubbing or hand cleansing prior to any patient contact such as Accent Plus Skin Cleanser; Accent Plus Perinal Cleanser; Bacti-Stat; Betadine; and Medi-Scrub. However, antimicrobial agents such as Accent Plus 1 Skin Lotion; Accent Plus 2 Body Massage; Accent Plus 2 Skin Crème; and Accent Plus Total Body Shampoo applied to the body of hospital personnel are not considered used in the treatment of the patient and the sale or use of these products is subject to tax.

(6) VITAMINS, MINERALS, HERBS, AND OTHER SUCH SUPPLEMENTS. In general, sales of vitamins, minerals, herbs and other such supplements are subject to tax. However, when vitamins, minerals, herbs and other such supplements are used in the cure, mitigation, treatment or prevention of disease, and are commonly recognized as a substance or preparation intended for such use, they will qualify as medicines for the purposes of Revenue and Taxation Code section 6369. As such, their sale or use is not subject to tax when sold or furnished under one of the conditions in subdivision (d)(1) through (d)(6).

(7) DIAGNOSTIC SUBSTANCES, TEST KITS, AND EQUIPMENT. Tax applies to the sale or use of diagnostic substances applied to samples of cells, tissues, organs, or bodily fluids and waste after such samples have been

removed, withdrawn, or eliminated from the human body. Diagnostic substances are applied to the samples outside the living body ("in vitro") in an artificial environment. They are not administered in the living body ("in vivo"). As the substances are not applied internally or externally to the body of the patient, they do not qualify as medicines under Revenue and Taxation Code section 6369.

Except as provided in Regulation 1591.1(b)(4), tax applies to the sale or use of test kits and equipment used to analyze, monitor, or test samples of cells, tissues, organs and blood, saliva, or other bodily fluids. Such items do not qualify as medicines regardless of whether they are prescribed for an individual by a person authorized to prescribe and dispensed pursuant to a prescription.

(f) INSURANCE PAYMENTS

(1) MEDICAL INSURANCE AND MEDI-CAL. The exemption of retail sales of medicines is not affected by the fact that charges to the person for whom the medicine is furnished may be paid, in whole or in part, by an insurer. This is so even though a joint billing may be made by the retailer in the name of both the person and the insurer.

(2) MEDICARE

(A) Medicare Part A. Tax does not apply to the sale of items to a person insured pursuant to Part A of the Medicare Act as such sales are considered exempt sales to the United States Government. Under Part A, the healthcare provider has a contract with the United States Government to provide certain services. Therefore, sales of medicines, devices, appliances, and supplies in which payment is made under Part A qualify as exempt sales to the United States Government.

(B) Medicare Part B. Tax applies to sales of items to a person in which payment is made pursuant to Part B of the Medicare Act. Sales made under Part B do not qualify as exempt sales to the United States Government even though the patient may assign the claim for reimbursement to the seller and payment is made by a carrier administering Medicare claims under contract with the United States Government. Under Part B, the seller does not have a contract with the United States Government. The contract is between the patient and the United States Government. Unless the sale is otherwise exempt (such as a sale of a medicine under subdivision (d)), the sale is subject to tax.

(3) EMPLOYER MEDICAL CONTRACTS. Certain employers have contracted with their employees to provide the latter with medical, surgical, and hospital benefits in a hospital operated by or under contract with the employer for a fixed charge. Usually the charge is by payroll deduction. These contracts are not insurance plans; rather, they are agreements to furnish specified benefits under stated conditions, one of which may be that no charge is to be made to the employee for prescribed medicines. The agreements may provide for making a charge for medicines furnished to out-patients but not to in-patients. This in no way affects the exemption of sales of medicines.

(g) RECORDS.

Any pharmacy whether in a health facility or not must keep records in support of all deductions claimed on account of medicines. Section 4081 of the Business and Professions Code requires that all prescriptions filled shall be kept on file and open for inspection by duly constituted authorities.

Pursuant to section 4081 of the Business and Professions Code, physicians and surgeons and podiatrists must keep accurate records of drugs furnished by them. Any deduction on account of sales of medicines shall be supported by appropriate records.

(1) The following written information constitutes acceptable documentation for retailers in those cases where sales are made of supplies which are "deemed to be dispensed on prescription" within the meaning of Revenue and Taxation Code section 6369:

Name of purchaser

Name of doctor

Date of sale

Item sold

The sale price

(2) "DOUBLE DEDUCTION" UNAUTHORIZED. The law does not, of course, permit a double deduction for sales of exempt medicines. For example, if an exemption is claimed on account of a sale of a prescription medicine, no additional deduction for the same sale may be taken as a sale to the United States Government under the Medicare Program.

(3) Persons making purchases of items in which their sale or use is exempt under this regulation should give their suppliers an exemption certificate pursuant to Regulation 1667.

History: Effective January 1, 1962.

Amended May 16, 1962.

Amended September 18, 1963, effective as amended September 20, 1963.

Amended and renumbered December 10, 1969, effective January 11, 1970.

Amended May 4, 1971, effective July 1, 1971.

Amended September 14, 1972, effective September 15, 1972.

Amended January 18, 1973, effective January 26, 1973.

Amended October 20, 1977, effective October 28, 1977. Changed to conform to Revenue and Taxation Code sections 6369 and 6369.2. Added orthotic and prosthetic devices to definition of "medicines"; excluded "dentures" from the definition of "medicines"; added mammary prostheses and ostomy appliances to items to be dispensed on prescription; added wheelchairs, crutches, canes, quad canes and walkers as exempt items. Changed all references to the term "hospital" to "health facility" as defined in section 1250 of the Health and Safety Code.

Amended March 1, 1978, effective April 29, 1978. In (b)(4) added list of specific orthotic devices; in (b)(5) added list of prosthetic devices; in (c)(1), (2) and (3) included specific items excluded from the term "medicines"; in (g) made grammatical change; in (i) added list of specific items to be included under this section; in (j) added leases to transactions to which tax does not apply and provided that tax applies to all replacement parts; in (m) deleted references to former section 280 of Title 17, California Administrative Code, and added (1) specifying acceptable documentation for exempt sales and (3) suggesting use of Regulation 1667 "Exemption Certificates."

Amended July 27, 1978, effective July 31, 1978. In (b)(5) deleted dental crowns, caps and inlays from definition of "medicines"; in (c)(1) added crowns, caps, inlays and other dental prosthetic materials and devices to exclusions from term "medicines"; in (c)(2) added orthodontic appliances to exclusions from term "medicines"; in (i) provided that orthotic and prosthetic devices shall be deemed to be dispensed on prescription; in (k) exempted replacement parts for wheelchairs, crutches, canes, quad canes and walkers from tax.

Amended September 27, 1978, effective November 18, 1978. In (b)(5) added intraocular lenses and ear implants; moved general exclusionary language from (c)(3) to (c); to (c)(2) added reference to footnote 3; and added reference to orthodontic appliances and devices to footnote 3.

Amended September 26, 1979, effective November 16, 1979. Adds (1); reletters former (1) and following subdivision.

Amended July 27, 1983, effective November 17, 1983. Added subdivision (b)(7); changed reference in first sentence of (c) from (b)(6) to (b)(7). Added "and, on or after January 1, 1983, "insulin syringes" to subdivision (h) and added subdivision (m); relettered former subdivisions (m), (n), (o) to (n), (o), (p).

Amended August 24, 1988, effective October 7, 1989. In subdivision (b)(4) added provisions to include "custom made biomechanical foot orthoses" within the definition of the term medicines.

Amended October 26, 1993, effective February 17, 1994. Amended subdivision (k) to provide the exemption from tax for white canes used by the legally blind; removed obsolete dates in subdivisions (b)(4), (b)(7), (h), and (m).

Amended June 27, 1996, effective August 23, 1996. Amended subdivisions (b)(4) & (5) to correct spelling errors; added new subdivision (n), and renumbered former subdivisions (n), (o), and (p) as (o), (p), and (q), respectively.

Amended November 19, 1996, effective December 19, 1996. Added new (a)(7) to incorporate provisions of Assembly Bill 3836 (Chapter 857, Statutes of 1994).

Amended August 10, 1998, effective October 17, 1998. Amended subdivisions (a)(6), (d), (e) to reflect changes in sections of the Business and Professions Code; corrected spelling errors in subdivisions (b)(4)(A) and (b)(5); changed "which" to "that" in subdivision (g); removed obsolete date in subdivision (k); amended subdivisions (l)(1) and (l)(3)(B) to reflect changes in sections of the California Vehicle Code.

Amended November 18, 1999, effective March 10, 2000. Deleted the references to sections 6369.1, 6369.2, 6369.4 and 6369.5 for those parts of former Regulation 1591 that were repromulgated as Regulations 1591.1, 1591.2, 1591.3 and 1591.4. Subdivision (a) formerly titled "Generally" was deleted and replaced with new subdivision (a) titled "Definitions." Subdivision (b) retitled "Medicines;" also added the phrase "the following items" to the end of the first sentence. Subdivision (b)(1) added new title "Preparations and Similar Substances" and amended language for clarity; new sentence added to the end of the first paragraph; also added new unnumbered paragraph. Subdivision (b)(2) added new title "Permanently Implanted Articles;" amended the first sentence for clarity; former second sentence deleted; new second and third sentences added; also two new unnumbered paragraphs added. Subdivision (b)(3) added new

title "Artificial Limbs and Eyes;" amended the first sentence for clarity; new last sentence added. Subdivision (b)(4) added new title "Orthotic Devices;" amended first sentence for clarity; deleted the part of the former first sentence after the semi-colon; deleted former second, third and fourth sentences and replaced them with new sentences which define when orthotic devices qualify as exempt medicines; examples (A), (B) and (C) consisting of items which do not qualify as custom-made biomechanical foot orthosis, were moved to become the new third unnumbered paragraph; the former second unnumbered paragraph, becomes the first unnumbered paragraph and is amended for clarity; new last sentence added; also new second unnumbered paragraph added. Subdivision (b)(5), added the title "Prosthetic Devices;" deleted the phrase "other . . . devices" from the first sentence and included its content in a new third unnumbered paragraph; added the phrase "are . . . 6369(c)(4)" to the end of the first sentence; also added new second, third and fourth sentences to the first paragraph; and new second and third unnumbered paragraphs added. Subdivision (b)(6) deleted and prior content moved to subdivision (b)(3). Former subdivision (b)(7) renumbered (b)(6) and retitled "Drug Infusion Devices;" added the phrases "a drug on . . . volume" and "qualify . . . section 6369(c)(6)." to the first sentence; also added a new second sentence. Subdivision (c), deleted the word "Term" in the title and replaced it with the phrase "the Definition of;" in the first paragraph deleted the cross-reference "(b)(2) through (b)(7) above" and replaced it with "subdivision (b)" in the first sentence; remainder of first sentence amended for clarity; also new second sentence added. In subdivision (c)(1) added cross-reference to new subdivision (b)(6). Subdivision (d) formerly titled "Who is a Registered Pharmacist" was deleted and its content transferred to new subdivision (a)(5) titled "Pharmacist." The language of former subdivision (a) "General" was moved to new subdivision (d) titled "Application of Tax – In General." New subdivisions (d)(1) through (d)(6) added. Subdivision (e) formerly titled "What Constitutes a Prescription" deleted and most of its content repromulgated as subdivision (a)(7). New subdivision (e) retitled "Specific Tax Applications." New subdivision (e)(1) added, detailing who can write a prescription. Subdivision (f) "Licensed Physician, Dentist or Podiatrist" renumbered as subdivision (e)(2). Subdivision (g) "Health Facility" renumbered as new subdivision (e)(3); the first sentence up to the colon deleted; also deleted the first unnumbered paragraph in former subdivision (g) and repromulgated it as (a)(4); and added the phrase "by a health facility" and a reference to (a)(4) in the first sentence. New subdivision (e)(4) added. New subdivision (e)(5) added to conform the regulation to the decision in Purdue Frederick Co. v. SBE (1990) 218 Cal.App.3d 1021 and to codify in regulatory form interpretations of the case now contained in annotations. New subdivisions (e)(6) and (e)(7) added. Former subdivisions (h) through (n) deleted. Former subdivision (o) redesignated as subdivision (f) "Insurance Payments." New subdivision (f)(1) titled "Medical Insurance and Medi-Cal" added, using the language of former subdivision (o). New subdivision (f)(2) titled "Medicare" added. Former subdivision (p) relettered (f)(3). Former subdivision (q) "Records," relettered (g); changed reference from section 4331 to section 4081 of the Business and Professions Code and added the words "and surgeons" in the second sentence; also changed the reference from section 4051 to section 4081 of the Business and Professions Code in first unnumbered paragraph. Subdivision (g)(1) added the phrase "Revenue and Taxation Code" to the first sentence. Subdivision (g)(3) added the phrase "in which their sale or use is" to first sentence; also changed the term "exempt" to "not taxable."

Amended December 13, 2000, effective April 12, 2001. Subdivision (b)(1), unnumbered paragraph – third and fourth sentences added to include liquid nutrition products in the definition of "substances and preparations." Subdivision (b)(2), first unnumbered paragraph, phrase added to clarify that dental implant systems, including dental bone screws and abutments are considered "permanently implanted articles." Subdivision (b)(5), fifth and sixth sentences added to clarify that specified devices used to administer liquid nutrition are included in the term "prosthetic devices."

Amended December 4, 2003, effective February 25, 2004. Subdivision (b)(2), second un-numbered paragraph - word "and" added before words "defillibrator programmer" and phrase "and tissue and breast expanders" deleted. Subdivision (b)(4) – word "ORTHODIC" corrected to "ORTHOTIC" in title. Subdivision (b)(5) – phrase "breast tissue expanders and tissue expanders" added to first un-numbered paragraph.

Regulations are issued by the State Board of Equalization to implement, interpret or make specific provisions of the California Sales and Use Tax Law and to aid in the administration and enforcement of that law. If you are in doubt about how the Sales and Use Tax Law applies to your specific activity or transaction, you should write the nearest State Board of Equalization office. Requests for advice regarding a specific activity or transaction should be in writing and should fully describe the facts and circumstances of the activity or transaction.